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SULFANILAMIDE: A REVIEW

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IT is now approximately three years since the new chemotherapeutic agent, prontosil, for the treatment of infections due to streptococci was presented to the medical profession. Whenever a new measure is introduced in therapeutics it is appropriate, after the accumulation of sufficient data, to review the evidence for and against its use, to learn especially the best method of application, and, most of all, to ascertain its limitations. In the case of sulfanilamide, the active principle derived from prontosil, this is particularly true because of the immediate enthusiasm with which it has been accepted.

Published articles on prontosil and its derivatives, including sulfanilamide, have been so numerous as to make it difficult to keep abreast of the subject. In fact, since Domagk's[1] original article, which appeared February 15, 1935, and which introduced prontosil for the treatment of hemolytic streptococcal infections in mice, two hundred and fifteen articles† on the subject had been published up to November 1, 1937. To be sure, it is still too early to evaluate all the possibilities and potentialities of this drug and to draw any far-reaching conclusions. Yet enough has been learned about its value in the treatment of certain conditions, the diseases in which its use has been unsuccessful and its definite toxic effects to warrant a brief résumé.

CHEMISTRY

The azo dyes, from which prontosil and sulfanilamide are derived, have been utilized in the textile industry for the past twenty-five years as dyes for cotton, wool and silk. In this industry it has been known for a long time that azo dyes form an intimate combination with the cellular protein. While studying this interesting phenomenon, Eisenberg[2] tested the behavior of one of these dyes, chrysoidin, on bacteria in vitro, and found it to have a strong bactericidal action. It was thus introduced as a chemotherapeutic agent, and subsequently various other azo compounds, trypan blue and so forth, were tried, particularly as urinary disinfectants, but with equivocal therapeutic results.

In 1932 Meitzsch and Klarer, while investigating chrysoidin, synthesized a chloride of the sulfonamide of chrysoidin, producing 4-sulfamido-2-4-diaminoazobenzene hydrochloride.† This was a red crystalline powder, slightly soluble in water, with a melting point of from 247 to 251°C. It was this substance that Domagk demonstrated in 1935 as exerting a protective action when given intravenously to mice infected with streptococci. He called the substance prontosil.

Unfortunately there are three substances with the name prontosil, and this has caused much confusion in the medical literature. The first is the monohydrochloride synthesized by Meitzsch and Klarer. The second is the dihydrochloride (4-sulfamido-2-4-diaminoazobenzene dihydrochloride) which is slightly more soluble in water and is just as effective. The dihydrochloride is also known as Prontosil Flavum, Prontosil Tablets and Rubiazol (a French preparation). The third prontosil is the disodium sulfonate salt (4-sulfamidobenzene-2-azo-l-hydroxy-7-acetylamino-naphthalene-3, 6-disodium sulfonate). The dihydrochloride salt is commonly used in Europe; the red prontosil solution employed in this country is the disodium salt in 2.5 per cent solution. This is also known as Prontosil Red, Prontosil Soluble, Prontosil S and Prontosil Solution. There was immediate and widespread interest in the use of these substances in both human and experimental infections caused by streptococci. In general the results were favorable.

The next important development came from Tréfouël, Tréfouël, Nitti and Bovet.[3] In their experimental work with prontosil they demonstrated that the azo linkage was not necessary in the molecule, but that the substance probably responsible for the

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†Courtesy of Winthrop Chemical Company and American Chemical Society.

†Deutsches Reich Patent 607537 of Dec. 25, 1932 and additional patents. D. R. P. 610320 of Dec. 1, 1933 and D. R. P. 638701 of Apr. 19, 1934.

action of the chemical was para-aminobenzenesulfonamide. Shortly thereafter Colebrook, Buttle and O'Meara,[4] and Fuller[5] in England, and Bliss and Long[6] in the United States demonstrated that prontosil is probably broken down to para-aminobenzenesulfonamide in the human organism. This is now considered the effective agent. This pertinent fact has prompted the Council of Pharmacy and Chemistry of the American Medical Association[7] to accept para-aminobenzenesulfonamide as an active chemotherapeutic substance in the treatment of infections due to hemolytic streptococci. Because this and related compounds were appearing on the market under a great variety of different names, the council selected "sulfanilamide" as the accepted name.[8]

Sulfanilamide is also used under the nomenclature of Prontosil Album and Prontylin. It is a white crystalline substance, readily soluble in hot water, hot alcohol and cold acetone, only slightly soluble in cold water and cold alcohol, and insoluble in ether, benzene and chloroform. It is neutral to litmus in an aqueous solution. For clinical purposes sulfanilamide has the desirable qualities of being easily administered and absorbed, when given by mouth, and is relatively inexpensive and of low toxicity.

MODE OF ACTION

When sulfanilamide is administered to mice immediately after experimental infection, it has a protective action so long as the chemical is given. It may protect the animal from several thousand minimal lethal doses of streptococci. If administration of the drug is delayed for several hours, however, or if the treatment is stopped before the animal recovers, it invariably dies. This demonstrates a bacteriostatic (growth-arresting) effect on the organism, although the exact site and mode of action are still unknown. Such an effect on streptococci in vitro has been shown in many experiments. A strongly bactericidal (organism-destructive) action has not been demonstrated in vitro or in vivo, except perhaps in the urine. Bliss and Long[9] believe that sulfanilamide acts by inhibiting the growth of hemolytic streptococci, perhaps injuring the organisms in such a way as to permit them to be phagocytosed by the white blood cells. Leukocytes are essential in the action of this drug, but whether its effects are primarily on the bacteria or on the white blood cells has not been determined.

Various other hypotheses have been advanced to explain the mode of action of sulfanilamide. These include injury to the capsule of the organism, inhibition of toxin formation and specific activation of the reticuloendothelial system. The protective action of the blood following sulfanilamide administration may be supplemented by that of the tissues of the whole animal, as suggested by Colebrook, Buttle and O'Meara.[4] This notion of body immunity as a factor is further suggested by recent observations that, while first infections of gonorrhea do not respond to the treatment, after an individual has had the disease for a time, good therapeutic results may be obtained.

EFFECTS ON BODY TISSUES

Until the accidental deaths caused in October, 1937, by sulfanilamide in diethylene glycol solution (Elixir of Sulfanilamide — Massengill), little study has been made of the organs of animals purposely killed by this drug. Hawking[10] gave toxic doses of sulfanilamide to rabbits and cats, and in those that recovered he found no histologic changes in the liver, kidneys or other viscera. Those animals which died from very large doses showed slight degenerative changes in the central nervous system in the form of chromatolysis in neurons of the anterior columns of the spinal cord, and in some of the nerve cells of the cortex and midbrain. In mice, Hageman[11] found some hemosiderin deposition in the spleen and slightly increased eosinophilia in the bone marrow.

Sulfanilamide could not be blamed as the cause of death in the patients who died after taking Elixir of Sulfanilamide. Necropsies and animal experiments showed that the cause was the diethylene glycol used as a vehicle. In the control studies on this problem done by Cannon,[12] two dogs and four rats were given sulfanilamide alone to see whether any tissue changes occurred. One dog and none of the rats experienced toxic manifestations. Autopsy revealed slight microscopic changes in the kidneys, consisting of moderate fatty degeneration in some of the collecting tubules of the dogs, but minimal in the rats. The livers of both dogs and rats showed no hydropic degeneration and practically no fatty changes. Sufficient observations on the organs of patients dying after sulfanilamide had been administered have not appeared. Although many of the clinical results reported following sulfanilamide treatment have been striking, its effect on body tissues in terms of late pathologic changes caused by this drug remains for the future to disclose.

CLINICAL USE

At present the clinical use of sulfanilamide is necessarily almost wholly empirical because the site and exact mode of action are not known. In the human subject, by any route of administration, the drug is readily absorbed and quickly diffused through the tissues. In this respect it is

similar to alcohol and urea.[13] Because of its ready diffusibility it attains a wide distribution, having been found in the cerebrospinal fluid, pleural fluid, prostatic secretion, saliva, pancreatic juice and bile in concentrations slightly lower than that of blood. On the other hand, the heart muscle, skeletal muscle, liver, lung and spleen contain a concentration nearly equivalent to that of the blood, whereas the skin and brain contain less, and bone and fat only small amounts. This information has encouraged the use of the drug in practically all types of inflammation involving the above secretions and due to causes even far removed from the original intention, in other words, as a therapeutic agent in infections due to hemolytic streptococci. For clinical use, the Council of Pharmacy and Chemistry has accepted sulfanilamide only for the treatment of infections due to beta-hemolytic streptococci of Lancefield's serologic Group A, although it has been found to be effective against a few other organisms.[7]

Certain observations have been of the greatest importance in establishing a rational basis for the treatment of infected human subjects. Unless the illness is critical and treatment must therefore be begun promptly, it is advisable to isolate and identify the infecting organism first, and with it test the effect of the drug in vitro. The action of the drug is better in vivo than in vitro, particularly against virulent strains of hemolytic streptococci; consequently, if sulfanilamide is effective in vitro, good clinical results may be expected.[14] Evidence for this is the fact that in beta-hemolytic streptococcal infections in human beings where treatment with sulfanilamide failed, subsequent in vitro experiments with the isolated organism have shown the drug to be ineffective as a bacteriostatic agent.

A level of from 7 to 10 mg. of sulfanilamide per 100 cc. of blood is optimum in obtaining the desired therapeutic effect. Little may be expected if the blood level is less than 5 mg. per cent. The rate of absorption of the drug from the gastrointestinal tract or from muscle is quite rapid, occurring within three to five hours. When given subcutaneously the dye may appear in the urine in fifteen minutes. Balance studies done on human subjects[15] indicate considerable individual variation, but in general when the drug is given in divided doses it takes from two to three days to establish equilibrium between the amount ingested and the amount excreted; when it has been discontinued, it takes about the same length of time to free the organism of the chemical. With normal kidneys, the drug is excreted almost wholly in the urine. In the case of decreased renal function, urinary excretion is diminished, and continued administration of sulfanilamide results in its accumulation in the body. Furthermore, toxic effects are not uncommon. These principles are necessary guides in the use of sulfanilamide in the treatment of human infections.

Method of Determination in Blood and Urine. The determination of the quantity of sulfanilamide in blood, urine and body fluids is advisable in every case where this drug is used. The method, originally devised by Marshall et al.[15] is simple enough for routine clinical use.

Procedure for Blood. Two cubic centimeters of oxalated whole blood is measured into a flask and laked with 16 cc. of 0.05% aqueous solution of saponin. Shake and allow to stand for 2 minutes. Add 2 cc. of 20% trichloracetic acid, shake, allow to stand 1 minute, and filter. Ten cubic centimeters of the filtrate is measured into a small flask and 1 cc. of 0.1% sodium nitrite solution that has been freshly prepared is added. Allow to stand 3 minutes, then add 5 cc. of a solution of dimethyl-alpha-naphthalamine (1 cc. of concentrated dimethyl-alpha-naphthalamine dissolved in 250 cc. of 95% of ethyl alcohol). The result will be a purplish-red azo dye, the amount of color produced being directly proportional to the amount of sulfanilamide present in the fluid analyzed.[16] Compare with standard.

Procedure for Urine. Dilute 1 cc. of urine to a 60-cc. volume with distilled water. Measure 10 cc. into a flask and add 1 cc. of 20% trichloracetic acid and 1 cc. of 0.1% sodium nitrite, and allow to stand for 3 minutes. Add 5 cc. dimethyl-alpha-naphthalamine (1 cc. in 250 cc. of 95% of ethyl alcohol). After 10 minutes, compare with standard.

Standard. Add 1 mg. sulfanilamide to 18 cc. of 20% trichloracetic acid and make to a volume of 100 cc. with distilled water. Treat 10 cc. of this solution exactly as outlined under blood. Place in a Duboscq colorimeter cup with vernier scale at 20 mm. and compare the unknown.

Calculation:

$$\frac{20}{X} = \text{mg. per cent sulfanilamide, where "X"}$$

is the reading of the unknown.

If the solution of blood or urine contains too large a quantity of chromogen for comparison, the appropriate dilution of filtrate can be made.

Oral Administration. The method of choice in the administration of sulfanilamide is by mouth. With this method it is usually easiest to maintain the blood level at from 7 to 10 mg. per cent. Sulfanilamide, or prontylin, is put up in tablet form, 0.3 gm. (5 gr.) and 0.5 gm. (7.5 gr.), mixed with an excipient for oral use. The daily dose for the average human adult has been expressed in terms of body weight, 0.1 gm. per kilogram or 1 gm. for each 20 lb.; but regardless of weight, the total dose per day should not exceed 5 gm., as toxic effects may result. In children, to maintain the optimum blood level 0.15 gm. per kilogram of

body weight may be necessary, and seems to be well tolerated. Several tablets are to be given at intervals of from four to six hours. In critical illness, such as streptococcal septicemia or meningitis, from 4 to 5 gm. may be given in the first four or six hours in order to obtain the desired blood level. The dose may then be reduced daily as the fever subsides and the patient improves. Owing to the tendency of streptococcal infections to recur, the drug usually must be given until the patient is well on the way to recovery.

A second method of administration used where the patient is not critically ill, as in urinary infections, is to begin with smaller doses, as 2.0 gm. (30 gr.) the first day, 2.5 gm. the second, and so forth, increasing the dose until the desired blood level has been obtained.

In patients with nausea, vomiting or coma, in whom administration by mouth is impractical, parenteral routes may be used.

Parenteral Administration. For parenteral administration, two substances are available, the red prontosil (disodium salt) solution for intramuscular use, and the white crystalline sulfanilamide powder, within its limits of solubility, for subcutaneous or intrathecal injection. The tablet for oral use cannot be dissolved for parenteral administration.

Although used rather extensively when the drug was first placed on the market, the red prontosil solution for intramuscular injection has become less popular than formerly. When given, it is used in patients weighing less than 150 lb. on the basis of 1 cc. per pound of body weight as the total daily dose, to be given at six-hour intervals. In individuals weighing more, the dose is 0.75 cc. per pound of body weight. Prontosil in this form colors the skin and the urine from pink to red. It has been found inadvisable in intraspinal therapy.[17] Prontosil is thought to be decomposed in the body with the formation of para-aminobenzenesulfonamide.

The sulfanilamide powder is soluble up to 0.8 per cent in physiologic saline, and is used in this form for subcutaneous and intrathecal injections. It is best to prepare the solution each day, even though it is fairly stable when kept at room temperature, because if it is placed on ice, the sulfanilamide rapidly crystallizes out of solution. To prepare such a solution, bring 100 cc. of sterile physiologic saline to a boil, add 0.8 gm. of the white crystalline powder and dissolve by the aid of shaking; inject when the solution has cooled to 37°C. The dose for hypodermoclysis is as follows: for individuals weighing up to 40 lb., 100 cc.; from 40 to 80 lb., 200 cc.; from 80 to 120 lb., 300 cc.; and over 120 lb., 400 cc. A satisfactory initial dose for adults is from 400 to 700 cc. The dose for intraspinal injection is from 15 to 30 cc. at from six- to eight-hour intervals. Slightly more cerebrospinal fluid than the quantity of sulfanilamide solution to be injected having been removed, the latter should be administered by gravity method, never under pressure. This solution has also been advocated for rectal administration; the amount of the dose, however, cannot be accurately given, as the rate of absorption of sulfanilamide from the colon and rectum is unknown.

The red prontosil or the sulfanilamide saline solution should never be given intravenously, since the excretion of the drug by the kidneys is so rapid that an adequate level of concentration in the blood is difficult to maintain. This method of administration is unnecessary, as the oral or subcutaneous routes are very effective in clearing the blood stream of susceptible organisms. Furthermore, untoward reactions are common when the drug is given by vein.

STREPTOCOCCAL INFECTIONS

Sulfanilamide and its related compounds were originally introduced for the treatment of infections due to beta-hemolytic streptococci, and are effective against most strains of this organism, but not all.[14] Results from this drug in the treatment of bacteremia and septicemia are favorable in that the blood stream may be cleared quite rapidly of the streptococci. However, isolated foci of streptococcal infection that may exist with the septicemia may not be affected.

Without a critical classification of the invading organisms, sulfanilamide and related substances have been used in the treatment of erysipelas, puerperal sepsis, tonsillitis, peritonitis, scarlet fever, meningitis, otitis media, Ludwig's angina and osteomyelitis. In throat infections, peritonitis and osteomyelitis (except isolated instances of mastoiditis), the effects of treatment with this drug alone have not been remarkable. The other conditions will be considered separately.

Erysipelas. In erysipelas and streptococcal cellulitis, good therapeutic results have been obtained. Of the many studies reported in the literature, one of the largest and best controlled is that of Snodgrass and Anderson.[18] These authors treated a total of 312 cases, and found that the prontosil they used promptly reduced the fever, prevented spread of the infection and decreased the duration of the toxemia. Old and young alike with this condition tolerated the drug well. Sulfanilamide seemed effective in decreasing the complications that follow erysipelas, but it did not necessarily prevent recurrences. When it is given orally, other therapeutic measures such as ointments are unnecessary.

The local application of the drug to the skin is useless.

Puerperal Infection. Reports of the results from sulfanilamide in the treatment of puerperal sepsis have been favorable. When the drug is given by mouth, it appears to prevent spread to the parametrial tissues, and septicemia is less apt to develop. Although difficult to evaluate, the mortality figures are given as reduced from about 25 per cent to from 5 to 8 per cent.[19] With the usual methods of treatment for puerperal sepsis, organisms may be found present in stained smears from the cervix for as long as three or four weeks after recovery. The same is true after treatment with sulfanilamide, so that cervical smears are not necessarily a criterion.

Scarlet Fever. Results in the treatment of scarlatina have not been so striking. In the few reports available most cases have recovered, but the institution of sulfanilamide therapy during the acute stage of the illness did not appreciably accelerate the rate of recovery.[20] In a series of 150 cases reported by Peters and Havard,[21] proseptasine — an English preparation, para-benzylaminobenzenesulfonamide — decreased the number of complications by about 20 per cent, but the patients treated had fever twelve hours longer than did the patients used as controls. The complications that may develop after scarlatina, such as otitis media, erysipelas and signs of renal damage, may respond favorably.

Streptococcal Meningitis. Sulfanilamide has proved its value clinically in this condition. Heretofore this disease was almost invariably fatal; with sulfanilamide treatment, reports[17, 22, 23, 24, 25] of cases recovered are appearing with great rapidity. The oral use of the drug may be supplemented by intraspinal injection. In this combination Schwentker, Clason, Morgan, Lindsay and Long[17] advise the oral dose in smaller amounts than usually used, with treatment continued at the advised blood level for at least two days after the spinal fluid has been rendered sterile and a definite improvement has been seen. Because of the possibility of relapse, they also advise oral administration until the patient is entirely well.

MENINGOCOCCAL INFECTIONS

In infections of the meninges by the meningococcus, sulfanilamide has been responsible for the saving of lives. While the results are not so startling in some cases as in cases of streptococcal meningitis, as the data of larger series are reported a definite decrease in the mortality rate is being shown. Sulfanilamide is effective against Types I and II of the meningococcus, which may be an advantage over serum therapy. In the latter, a polyvalent serum may not contain the specific antibodies against the particular strain infecting a given patient. In a further comparison, Brown[26] has demonstrated that the protective influence of 8 mg. of para-aminobenzenesulfonamide is comparable to 0.1 cc. of highly potent antimeningococcal serum. Serum may be used alternately with sulfanilamide given intraspinally.

In the meningococcemia associated with meningitis, sulfanilamide by mouth is effective in rapidly clearing the blood stream of organisms. Very few reports of meningococcemia without meningitis treated with sulfanilamide have been made to date.

GONOCOCCAL INFECTIONS

As was to be expected because of the close biologic relation of the gonococcus to the meningococcus, sulfanilamide was applied to the treatment of gonorrhea after beneficial results had been obtained in meningococcal infections. The first reports were extremely favorable, but as data accumulate more and more failures occur. Ninety per cent cures have been reported by Reuter,[27] and the Mayo Clinic[28] gives 90 per cent for male and 80 per cent for female patients. Instead of simply dividing the cases into acute and chronic, Herrold[29] paid particular attention to first infections and found that the patients respond poorly if at all. All so-called cures in his series were in patients who had had gonorrhea for some time. In a more recent report[30] of 72 cases treated and adequately followed, there were 12 complete failures and only 14 cures.

Sulfanilamide may cause the organisms to disappear from the stained smears in from two to six days. However, this may give a false sense of security to both patient and physician as to adequate treatment and cure. It is apparently effective in some cases in preventing an extension of the infection to the posterior urethra and prostate.

In the chronic cases, in which the drug seems to be the most effective, Dees and Colston[31] originally outlined the oral dose as follows: 4.8 gm. daily for two days, 3.6 gm. for three days, and 2.4 gm. for from four to eight days. More recently Walther[32] has considered this dosage too large, and has advised beginning with smaller doses and gradually increasing the amount: for example, 1.2 gm. for two days, 2.4 gm. for two days and an increase to 4.8 gm. daily as tolerated. It is unwise to attempt the treatment of gonorrhea by the injection of sulfanilamide into the urethra.

The results in the treatment of gonococcal arthritis have been too few to warrant definite conclusions. Keefer[33] has found it possible to sterilize the synovial fluid within two days after the oral

administration of sulfanilamide. He considers this evidence that sulfanilamide may be effective in the treatment of gonococcal arthritis, particularly in patients with an infected synovial fluid. Keefer's studies[34] have shown further that after several days' treatment the blood becomes bactericidal as well as bacteriostatic. That the drug does not hinder natural immunologic processes is suggested by the failure of sulfanilamide to influence the gonococcal complement-fixation reaction of the blood.

PNEUMOCOCCAL INFECTIONS

Domagk's original report stated that prontosil was ineffective against pneumococci, and Hörlein's[35] later communication revealed equivocal results. In experimental pneumococcal infections in animals, rats, mice and rabbits have varied in their responses to sulfanilamide, with conflicting conclusions resulting. Pneumococcal pneumonia in the rat approximates most closely that seen in the human subject, and in experiments with this test animal the drug has been effective in combating Types I, II, III and XIV. In patients, however, the results have not been striking. Most conservative clinicians have been satisfied to treat Types I and II with serum. As a result, no adequate series of cases treated with sulfanilamide has appeared. With serum not yet available, Heintzelman, Hadley and Mellon[36] have shown good results in the treatment of the highly fatal Type III with sulfanilamide. In their series of 19 cases, of which 9 were treated and 10 were controls, 7 treated patients recovered, a mortality of 22 per cent. With 23 cases in their community added to the untreated cases, 9 patients recovered, a mortality of 73 per cent. Many more data are essential, however, before sulfanilamide can be accepted as an effective therapeutic agent in the treatment of pneumoccocal pneumonia.

In other infections due to pneumococcus, such as otitis media and mastoiditis, sulfanilamide may be of benefit.[37] A temporary improvement in patients with pneumococcal meningitis with a reduction in the organisms and cells in the cerebrospinal fluid has been noted, but no recoveries following sulfanilamide therapy have been reported.

URINARY TRACT INFECTIONS

Sulfanilamide has proved of distinct value in the treatment of certain infections of the urinary tract. Marshall, Emerson and Cutting[38] compared the renal clearance of sulfanilamide with a simultaneously obtained creatinine clearance, and found the former from 20 to 30 per cent of the latter. Their studies indicate that the drug is excreted entirely by glomerular filtration and that from 70 to 80 per cent of it is reabsorbed by the tubules. The concentration in which it is excreted depends upon the amount administered and upon the function of the kidneys.

Helmholz and his co-workers[39, 40, 41, 42, 43] at the Mayo Clinic have made extensive studies with sulfanilamide in the treatment of urinary sepsis. In the human subject, sulfanilamide is excreted in the urine chiefly in two forms, in the free state and as para-acetylaminobenzenesulfonamide. The experiments of Helmholz and Osterberg[43] indicate that concentrations of free sulfanilamide of from 30 to 40 mg. per 100 cc. of urine are necessary in order to obtain good bactericidal action, but occasionally even at lower concentrations there is a bacteriostatic effect. From 3 to 4 gm. of sulfanilamide a day gives a urinary excretion of from 60 to 125 mg. of free sulfanilamide and from 50 to 100 mg. conjugated as the para-acetyl salt. In the case of impaired kidney function the drug is excreted in the urine in lower concentrations, so that it is retained in the blood stream to give a higher blood level, which may result in toxic manifestations. However, when used cautiously (Helmholz and Osterberg) a lower urinary concentration of the drug has been found effective in treating infection of the urinary tract in spite of an elevated blood urea nitrogen.

Sulfanilamide given by mouth has been found effective in the treatment of urinary sepsis due to *Staphylococcus aureus, Bacillus coli* and *Aerobacter aerogenes,* and in some cases due to *Proteus vulgaris* and to *Pseudomonas seruginosa.* In infections due to *Streptococcus fecalis* the drug is ineffective. In general, bacillary infections respond more favorably than do those due to cocci.

Sulfanilamide is usually more effective in an alkaline than in an acid urine. Consequently, it may be advisable to administer from 0.3 to 0.6 gm. (5 to 10 gr.) of sodium bicarbonate with each dose. In order to act in an acid urine the concentration of sulfanilamide must be higher than in the case of an alkaline urine.

An effective dose by mouth, as outlined by Helmholz, consists, in adults, in 2.0 gm. the first day, 2.6 gm. the second day, 4.0 gm. the third day and so on, with a gradual decrease as the desired blood and urinary concentrations are obtained and good clinical results are observed. In general, patients taking larger doses show a more satisfactory response. The daily dose for infants is from 0.3 to 0.6 gm., and for children of twelve, 2.0 gm.

In comparing sulfanilamide with the recently introduced mandelic acid in the treatment of urinary tract infections, Helmholz[44] points out that each has its place. The advantages of sulfanilamide are that it can be used in acute infections,

that it is the drug of choice in the average case, and that it is usually easier to get a urine slightly alkaline for sulfanilamide action than to obtain a pH of 5.5 necessary for mandelic acid. Thus, with one drug acting only in an acid medium and the other giving the best results in an alkaline medium, the two supplement each other, and should be used in the treatment of urinary infections according to the organisms causing them.

OTHER ORGANISMS AND INFECTIONS

The widespread enthusiasm over sulfanilamide and its therapeutic possibilities has caused it to be tried in almost every type of infection, even far removed from those due to the streptococcus. Many of the studies have been confined to the test tube, where the effect of this drug has been tried on *Bacillus typhosus, B. paratyphosus A and B, B. dysenteriae* (Flexner, Shiga) and related gram-negative bacilli,[45] and *Hemophilus influenzae*[46] without any action.

In animal experiments with mice, Buttle and his associates[47] found sulfanilamide to give some protection against *B. typhosus, B. paratyphosus B, B. aertrycke,* Friedländer's bacillus, *Pasteurella pseudotuberculosis* and *P. septica.* In the same animal it is ineffective against the viruses of encephalitis (St. Louis type) and of benign lymphocytic choriomeningitis.[46] Prontosil was effective in rabbits in infections caused by the latter but ineffective in herpes-virus infection and also in that due to the virus of lymphogranuloma inguinale in monkeys.[48] In the rabbit, sulfanilamide had no effect on *Treponema pallidum.*[49]

In human patients, sulfanilamide has been found to be relatively ineffective in staphylococcal infections (except in the urine), *Streptococcus viridans* endocarditis, rheumatic fever and chorea. Massell[50] found a failure of the drug to prevent the recurrence of rheumatic fever after streptococcal sore throat treated with sulfanilamide. In the treatment of gas gangrene due to *B. welchii* the drug has met with some degree of success.[51] In a few cases it has been reported as effective in the treatment of malaria, both acquired[52] and induced.[53]

In mixed infections, such as those due to streptococci and staphylococci, the drug may be of benefit. Equivocal results have been reported in the treatment of streptococcal infections complicating tuberculosis.[54] Isolated instances have occurred in which the condition of patients with tuberculosis has been made definitely worse by sulfanilamide.

TOXIC EFFECTS

Untoward reactions, even death, may result from the administration of sulfanilamide, a fact which in several communities has prompted legislation regarding the sale and use of this drug.[55] The toxic effects are more commonly the result of its indiscriminate use, but may occur from an idiosyncrasy to it. They may be classed as of three types: mild, moderate and severe. The mild symptoms consist of headache, anorexia, vertigo and general malaise, with possible slight cyanosis and dyspnea. The moderate reactions may be classed as a progression of any of the foregoing symptoms, with special reference to cyanosis and dyspnea. The severe reactions may result in persistent sulfhemoglobinemia, skin manifestations, hyperpyrexia or hypopyrexia, abdominal and chest pains, tachycardia, persistent dyspnea, diarrhea and numbness and tingling of the hands and feet. Marked disturbances of the blood, such as anemia, jaundice, leukopenia and agranulocytosis, may occur. The severe manifestations may result in collapse and death.

A lowering of the blood-plasma carbon-dioxide-combining power commonly occurs following the administration of sulfanilamide.[56]

Buchtel and Cook[42] have found that 15 per cent of patients cannot take large doses of sulfanilamide, and 10 per cent are unable to tolerate it at all. Patients in bed tolerate larger doses than do those who are ambulatory. Several investigators have pointed out that ambulatory patients exposed to sunlight are more apt than are others to develop a skin rash after sulfanilamide. In general, children tolerate the drug better than do adults. Elderly patients with cardiac, renal or hepatic involvement cannot stand the larger doses as can others.

The commonest symptoms of sulfanilamide toxicity are cyanosis and dyspnea. Cyanosis occurs in about 75 per cent of patients receiving the drug, and may appear early. It is thought to be due to methemoglobin or sulfhemoglobin formation, or to a peculiar red-cell-binding pigment in the blood.[57] In the former case it is usually transient in character and does not have lasting effects. It can be determined spectroscopically, yielding a band at a wave length of 562 mμ. Sulfhemoglobinemia, on the other hand, as demonstrated by Colebrook and Kenny,[19] Discombe,[58] and Paton and Eaton,[59] is of a more lasting character and may be responsible for many symptoms and pathologic changes. It yields a band in the absorption spectrum at 620 mμ. Naturally, sulfhemoglobinemia can reduce the oxygen capacity of the blood, but it need not affect the hemoglobin content as determined by routine colorimetric methods.

According to the more recent studies of Archer and Discombe,[60] any preparations which are liable to produce a watery stool in the patient, such as magnesium sulfate and other cathartics, may ag-

gravate the deleterious effects of sulfanilamide in causing sulfhemoglobinemia. Hydrochloric acid and coal-tar derivatives may act similarly. Sulfhemoglobinemia, however, may develop from sulfanilamide therapy alone. Patients may develop both methemoglobinemia and sulfhemoglobinemia, but not usually at the same time.

The blood should be examined frequently for the possible development of anemia. A lowering of the hemoglobin and red-cell content of the peripheral blood occurs rather commonly after sulfanilamide administration. Severe anemias, as reported by Harvey and Janeway,[61] may result, and may be hemolytic or aplastic in character. These authors compared the anemia which they observed with the hemolytic crises produced by phenylhydrazine. It is of interest that in the cases of anemia reported by them, and similarly in those reported by Kohn,[62] as the anemia developed the white-cell count rose, with many immature forms present. In the necropsy study by Borst,[63] in which the patient died with agranulocytosis, study of the bone marrow was inconclusive.

That drugs possessing in common a benzene ring with an attached NH_2 or amine group, which increases the ease of oxidation, may cause agranulocytosis in susceptible individuals was suggested by Kracke.[64] This may be significant in regard to sulfanilamide, since it is such a benzene-ring compound, and since instances of agranulocytosis following its use have occurred. Serial leukocyte counts in patients receiving the drug may show either an increase or a decrease in white blood cells. In Borst's case of agranulocytosis the patient had had a previous blood disorder, which may have been a factor. Frequent white-blood-cell counts in the case reported by Young[65] gave no warning of the impending disaster.

When hyperpyrexia occurs as a toxic manifestation of sulfanilamide therapy, it may be difficult to tell whether it is due to the drug or to the infection for which it is being given. As described by Hageman and Blake,[66] it is usually abrupt in onset and may occur at any time. In their series it occurred in 21 of 134 cases, an incidence of 16 per cent. The reaction varies in intensity and the average duration is from two to four days, with prolongation in cases in which the drug is continued. Eosinophilia of from 1 to 6 per cent was present in about half their 21 cases. The condition may very closely simulate serum sickness; skin tests for sensitivity showed no positive reactions.

Skin rashes occurring after sulfanilamide are of various forms, simulating measles, scarlet fever, urticaria and erythema multiforme. They may resemble the reactions from the barbiturates.[67] The eruption occurs most commonly on the face, trunk and extremities, and may or may not be accompanied by fever. In certain ambulatory cases reported there seems to have been a definite relation between the development of a rash and exposure to sunlight. Positive skin tests have occasionally been reported.

Although tissue reactions to any appreciable degree have not occurred in animal experiments with sulfanilamide, nephropathies in human subjects have been reported. Colebrook and Kenny[19] state that 40 per cent of 38 patients studied showed red blood cells and casts in the urine, while 20 per cent had an increase in urinary albumin content over that originally present. Definite nephritis has been reported.[68] It may be difficult, however, to evaluate the relation of the nephropathy to the drug or to the infection, since Anghelscu et al.[69] and others have successfully treated cases of erysipelas with concurrent renal disease.

Treatment of Toxic Manifestations. The treatment of toxic manifestations from sulfanilamide administration depends to some extent on the nature of the reaction. Methemoglobinemia is a common finding, and the cyanosis alone does not contraindicate the use of the drug, but it must be continued cautiously. With all other types of reaction administration of the drug should be stopped. Because sulfanilamide is so rapidly and practically completely excreted in the urine, fluids should be forced. Archer and Discombe[60] have outlined certain principles for the prevention of sulfhemoglobinemia. They advise the use of no other drugs with sulfanilamide, except for sodium bicarbonate, employed in order to obtain an alkaline urine or to combat acidosis. The colon should be kept free from food residues by a cleansing enema before treatment is started, and a low-residue diet of adequate caloric value but containing few eggs should be given. When sulfhemoglobinemia occurs, the only treatment is blood transfusion. This is also the treatment for severe anemia, as liver and iron are apparently not effective. The administration of oxygen may be helpful in cases of methemoglobinemia.

SUMMARY

Sulfanilamide appears to have proved its worth as an effective chemotherapeutic agent in the treatment of certain infections. From the more important facts here summarized it can be clearly seen that it is not a panacea. Since there is no shorter road to the discredit of any drug than its indiscriminate use, emphasis has been placed upon methods of administration, dosages and toxic effects. Clearer indications and contraindications to its use and the possible deleterious effects of its

long-continued administration have yet to be disclosed.

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DISSECTING ANEURYSM OF THE AORTA

Two Cases with Unusual Features

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RECENT definition of the clinical course of dissecting aneurysm of the aorta has resulted in its more frequent recognition. Whereas up to 1935 the condition was diagnosed in but some half-dozen instances, an appreciable number of cases have been correctly diagnosed during the past three years.[1, 2, 3] Recognition of a case with a typical clinical course is no longer difficult. Indeed, the clinical picture may be specific. Cases with a "silent" or atypical course, on the other hand, usually escape recognition.

In the differential diagnosis, coronary thrombosis offers the main difficulty. The presence of syphilitic aortitis or aneurysm is considered by most writers[2] as evidence against the presence of dissecting aneurysm. The inflammatory reactions caused by syphilis tend to fuse the layers of the aorta, thereby making dissection difficult if not impossible. Syphilitic aneurysm usually becomes thinned out and ruptures without dissection.

The following 2 cases are reported because they demonstrate that dissecting aneurysm can cause coronary occlusion and myocardial infarction, and that syphilitic and dissecting aneurysm may coexist.

CASE REPORTS

Case 1. A 40-year-old, male Filipino was first observed in December, 1936. For 7 years he had experienced mild epigastric distress. For 6 months he had noted subcardiac and more severe epigastric distress, and had dyspnea and palpitation on exertion. The discomfort appeared after eating, was nonradiating and was relieved by soda. The day before entering the hospital he vomited coffee-ground material and on four occasions had tarry stools.

Physical examination revealed slight sclerosis of the vessels of the eyegrounds. The heart was slightly enlarged. The rhythm was regular. There was a soft systolic murmur. The aortic second sound was ringing. The arterial pressure varied from 168/106 to 178/120. The rest of the findings were unessential. The urine revealed no abnormalities. There was a severe degree of secondary anemia, with a red-blood-cell count of 2,400,000 and a hemoglobin of 34%. The white-blood-cell count was 13,800. The stools were tarry and the guaiac test was 4+. A blood Hinton test was negative. X-ray study of the gastrointestinal canal revealed changes diagnosed as gastric and duodenal ulcers. The electrocardiogram revealed changes consistent with digitalis effect. The rest of the tests were unessential.

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Following the use of Sippy diet and administration of iron, the gastric symptoms and the anemia decreased. The diagnoses were peptic ulcers, essential hypertension and a slight degree of arteriosclerosis.

After leaving the hospital the patient continued to feel well. He lost his position, however, because "high blood pressure" was discovered on routine physical examination. At 1:30 a. m. on November 2, 1937, he experienced sudden breathlessness and orthopnea, which continued for several hours. In the afternoon of the same day he developed sharp, burning, boring, nonradiating pain in the epigastrium. When he entered the hospital 2 days later he was weak and irritable. The radial pulse was imperceptible and the arterial pressure could not be measured. In a few hours he improved somewhat.

Physical examination revealed an anxious patient with slight cyanosis. The heart was moderately enlarged. The pulse rate was from 130 to 140 and regular. The sounds were weak. The pulmonary second sound was accentuated and the aortic second sound was barely audible. The blood pressure was 100/55. The lungs were normal. There was tenderness in the epigastrium, but no spasm. The other findings were irrelevant. The red-blood-cell count was 6,000,000 and the hemoglobin 95%. The white blood cells on two occasions numbered 27,600 and 21,300. The nonprotein nitrogen of the blood was 46 mg. per cent. The x-ray picture of the chest showed widening of the aorta. The electrocardiogram taken on November 4 showed T_1 and T_2 diphasic, T_3 upright, T_4 (chest electrode, fifth interspace 6 cm. from midline, and left leg) inverted (normal), and left ventricular preponderance. There was sinuauricular tachycardia, with a pulse rate of 107. The electrocardiogram was interpreted as indicating myocardial disease. The next day, however, T_1, T_2 and T_3 were diphasic and T_4 was inverted. There was a prolonged Q-T interval; K equaled 0.47 (Fig. 1). Because of changes in the T waves within 24 hours, an acute myocardial process, possibly coronary thrombosis, was considered likely, although the electrocardiographic changes were not characteristic of thrombosis. The rest of the laboratory findings were unessential. The general condition remained practically unaltered when, 2 days after admission, the patient suddenly collapsed, developed convulsions and died.

The differential diagnosis rested between coronary thrombosis and perforated gastric ulcer.

The essential findings at postmortem were as follows. The pericardial sac was distended and contained about 200 cc. of clotted blood. At the root of the pulmonary artery and the aorta there were extensive hemorrhagic extravasations into the adventitial tissue. The heart weighed 500 gm. The myocardium of the lateral aspect of the left ventricle was lighter than the normal portions and contained yellowish and reddish areas. About the mouths of both coronary arteries there was a marked degree of extravasation of blood. The left coronary artery was compressed near its opening by a dissection which extended to a distance of about 1 cm. from the orifice. The coronary arteries contained no thrombus.

About 1 cm. above the aortic valve there was a sharp, cleft-like rupture approximately 4 cm. in length, in-

volving the intima and the media. Nearby there was another slit in the aorta about 1 cm. in length. From the base of the aorta the wall was dissected down to the mouth of the celiac artery, where the dissection through the intima reruptured into the aorta. Below this point the aorta was intact. There was a small extravasation of blood into the posterior mediastinum. Scattered over the intima of the entire aorta there were small, raised, yellowish, atheromatous deposits.

Histologic examination of the myocardium revealed changes indicating acute infarction. The inner half of the myocardium of the left ventricle contained massive infiltration of the stroma by polymorphonuclear leukocytes. There was also occasional invasion of the muscle fibers, which showed hyalinization with karyolysis. Sections of the aorta revealed an essentially normal structure.

sinus rhythm with a rate of 79 per minute. The P-R interval was 0.16 second. T_1 was upright, T_2 low, T_3 inverted. There was left ventricular preponderance. The diagnosis was essential hypertension, and there was serologic evidence of syphilis.

The patient was admitted to the hospital on August 9, 1937, in a state of circulatory collapse. She was unable to give an adequate history. On the day of admission she suddenly experienced a severe, sharp pain in the middle of the back of her thorax. Subsequently the pain was felt in the substernal and subxiphoid regions. Because of the severity of the pain she was barely able to breathe. On physical examination she was found to be anxious and pale, and covered with cold, beaded perspiration. The heart rate was rapid and regular. The sounds were barely audible. The blood pressure was 60/40. The temperature

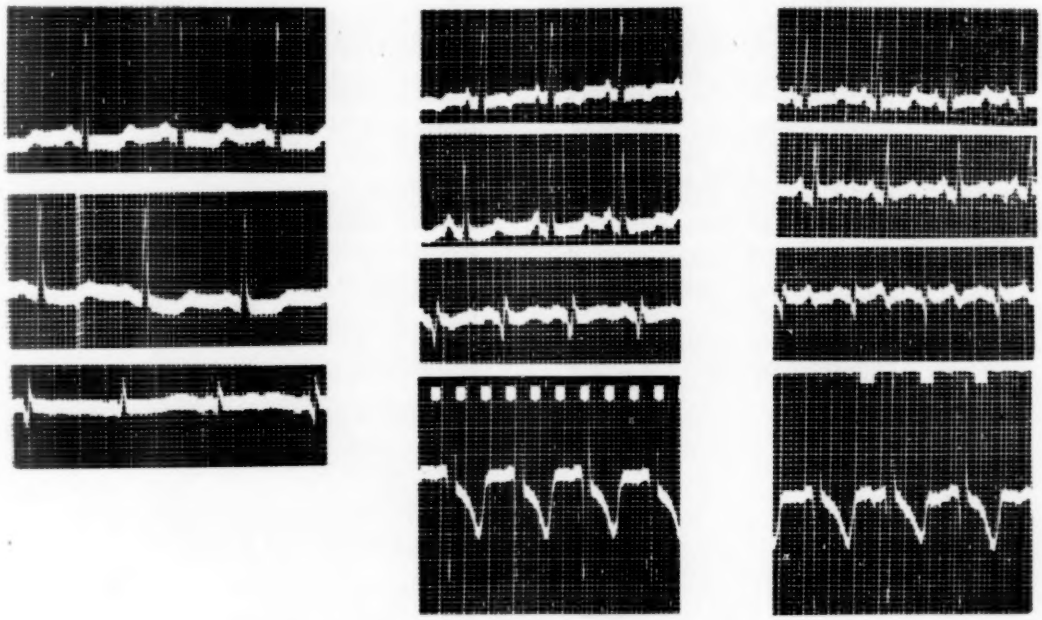

Figure 1. *Electrocardiograms in Case 1 before (12/8/36) and after (11/4/37 and 11/5/37) the onset of dissecting aneurysm, reproduced in respective order.*

The anatomic diagnoses were as follows: dissecting aneurysm of the aorta with hemopericardium; pulmonary congestion and edema; compression of the mouth of the left coronary artery caused by dissection of this artery; myocardial infarction of the left ventricle; healed chronic pyelonephritis; moderate atherosclerosis of the aorta; and healed cholecystitis.

Case 2. A 61-year-old, white woman was observed in the Outpatient Department on several occasions between July 9 and July 22, 1937. Her main complaints were insomnia and dizziness of 3 years' duration. She had known since 1925 that she had "high blood pressure." Her mother died of "high blood pressure" at the age of 55. One brother died from "lifting" at the age of 32. Her husband died insane.

Physical examination indicated a moderately enlarged heart with regular rhythm. There was an apical systolic murmur. The blood pressure on two occasions was 204/120 and 200/110. The rest of the examination was unessential. Blood Wassermann and Hinton tests were positive. An electrocardiogram on July 16, 1937, showed

was 99°F. The blood count showed 3,000,000 red cells, with a hemoglobin of 60% and 14,800 white cells. A blood Hinton test was positive. The electrocardiogram revealed normal sinus rhythm. T_1 and T_3 were upright, T_3 diphasic. The chest lead (chest electrode, fifth interspace 8 cm. from midline, and left leg) was diphasic (abnormal); there was left ventricular preponderance (Fig. 2). There were only minor changes since the electrocardiogram taken on July 16.

The day after admission the patient's condition was somewhat improved. The heart was found to be displaced to the right. Signs of fluid appeared in the left chest, and a tap yielded 50 cc. of bloody fluid. The patient failed to respond to oxygen and shock therapy and died on August 11. A diagnosis of luetic and arteriosclerotic heart disease with dissecting aneurysm was made.

The following were the pertinent findings at postmortem examination. The left pleural cavity contained about 1500 cc. of clotted blood. The left half of the posterior mediastinum was swollen because of the pres-

ence of considerable dark blood. At the level of the ninth thoracic vertebra there was roughening of the parietal pleura, which appeared to be the site of entrance of blood into the left pleural cavity. The tissues of the superior mediastinum were infiltrated with blood.

The heart weighed 380 gm. The aortic cusps were slightly thickened, but there was no separation of the commissures or interadherence of the cusps. The mouths of the coronary arteries were patent, with slight narrowing of the right coronary orifice. The upper fifth of the upper lobe of the left lung was voluminous, gray and crepitant. The remainder of the left lung was collapsed.

The entire thoracic aorta was dilated. At the junction of the arch and the descending aorta there was a saccular aneurysm, conical in shape and 6 cm. in height, directed upward and posteriorly (Fig. 3). The mouth of the aneurysm measured 5 cm. in diameter, and its center was situated 8 cm. from the origin of the left subclavian artery. The apex of the sac rested on the anterior aspects of the bodies of the second and third thoracic vertebrae, the latter of which was eroded to a depth of 1 cm. The aneurysm was almost completely filled with organized lamellated clots. The undilated part of the aorta at about the level of the center of the aneurysm was completely ruptured transversely. The margins of rupture were irregular. The mediastinal hematoma arose from this rupture. Beginning with the acute tear the aorta was dissected upward and downward between the media and adventitia. Downward the dissection ended at the level of the upper portion of the abdominal aorta. The intima of the aorta contained several atheromas from 0.1 to 1 cm. in diameter. Some of these were calcified. At the juncture of the old aneurysm and unruptured aortic wall along the margin of the rupture there was an area of softening 1.5 cm. in diameter, which might have been the surface of the original rupture. The rest of the findings were irrelevant.

Histologic examination of the aorta revealed the following. Section of the ascending aorta showed essentially normal structure. There was some increased vascularity. Sections of the arch were also normal. Sections obtained from the old aneurysm showed endarteritis with thickening of the adventitia. There was also perivascular infiltration with lymphocytes. There were scars and absence of elastic tissue in the media. These changes were considered as being consistent with a syphilitic process. The site of the acute rupture revealed normal margins, except for evidence of hemorrhage and infiltration by polymorphonuclear leukocytes of the layers between the intima and media. Section of the abdominal aorta revealed marked thickening of the intima and vascularization of the media below the atheroma of the intima.

The anatomical diagnoses were acute dissecting aneurysm of the aorta with hematoma of the mediastinum and with left hemothorax; old luetic aneurysm of the thoracic aorta; atherosclerosis of the aorta; and atelectasis of the left lung.

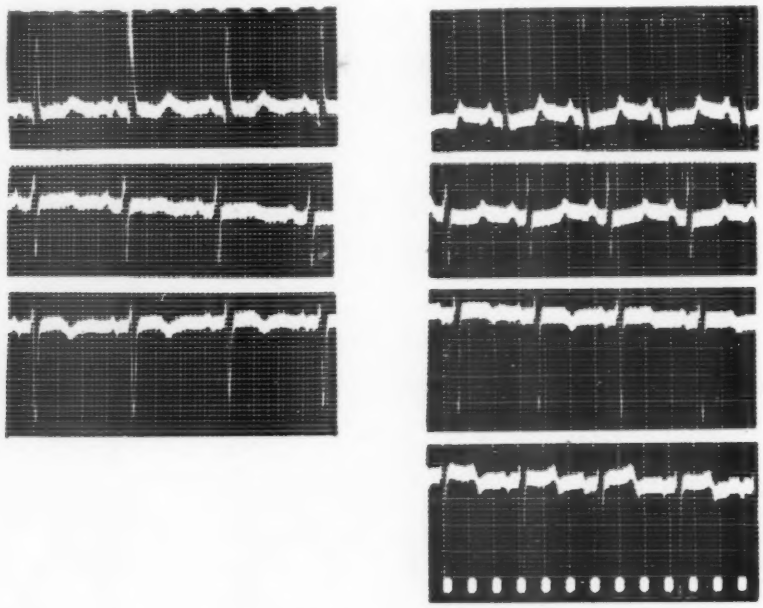

Figure 2. *Electrocardiograms in Case 2 before (7/16/37) and after (8/10/37) the onset of dissecting aneurysm, reproduced in respective order.*

DISCUSSION

A detailed description of the clinical course and of the functional and structural changes in dissecting aneurysm of the aorta has been given elsewhere.[2] As indicated, the condition should be considered as more than a medical "curiosity." The 10 cases previously reported occurred among 3206 necropsies, a ratio of about 1:320. Since this first report was published there have been, during the three years 1935 to 1937, inclusive, 11 additional cases among 2202 necropsies, a ratio of 1:200. It is of interest that in these 11 cases the condition was diagnosed 7 times clinically. The total number of correctly diagnosed cases available is about 15 since 1935, as contrasted with a total of 6 cases diagnosed up to that time.

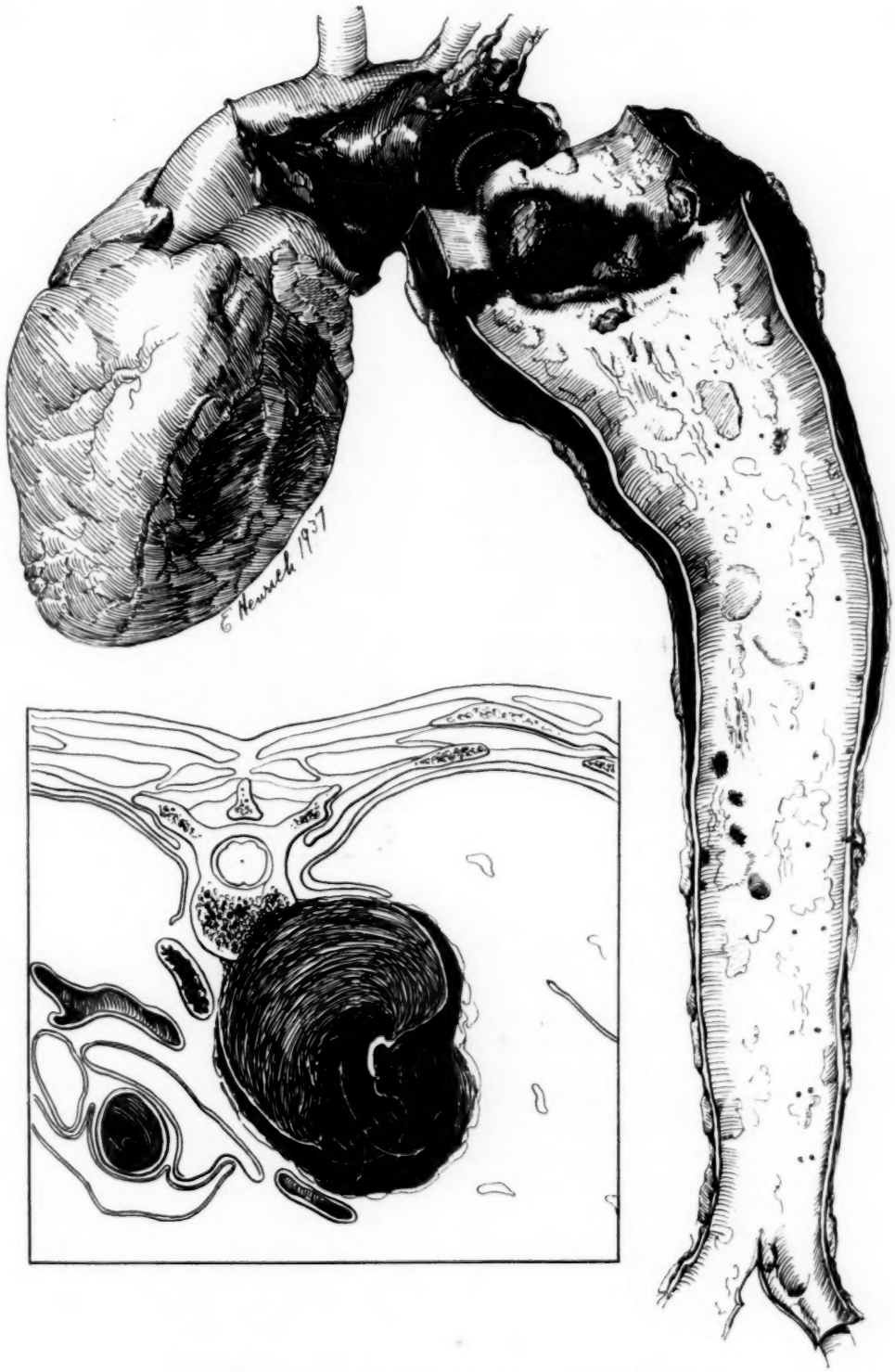

Figure 3. *Appearance of the aorta and of the opening of the old syphilitic aneurysm; acute tear of the intima leading to the dissection toward the base of the heart and to the abdominal aorta (upper picture). Transverse section at the level of the third thoracic vertebra, showing the relation of the acute dissection to the syphilitic aneurysm; note erosion of part of the vertebral body by the syphilitic aneurysm (lower picture).*

The onset of dissecting aneurysm is characterized by sudden thoracic pain, transient syncope, dyspnea, orthopnea and prostration with circulatory collapse. Depending on the direction and the extension of the dissection, examination may reveal manifestations of mediastinal compression and tumor, partial or complete occlusion of arterial vessels and functional disturbances resulting from occlusion of the nutrient arteries, such as hemiplegia, paraplegia, monoplegia, intestinal paresis and infarction, hematuria and, at times, anuria. Tenderness and widening of the abdominal aorta may occur. As a result of rupture of the dissection, signs of fluid may develop over the chest, particularly over the left pleural surface, or the syndrome of cardiac tamponade may appear. Distortion of the aortic cusps may be the cause of diastolic murmur over this area in about 20 per cent of instances. In one case without pulmonary infarction jaundice developed, presumably as the result of hematoma.

Following the initial tear, thoracic pain often travels downward, and subsequently abdominal pain may develop. Frequently the signs of arterial compression change during the course of the disease. Fever and hemoptysis are often present after the onset of the rupture. In contrast to these manifestations, there are rare instances in which the onset is silent and the dissection is compatible with relatively good functional capacity. Development of an endothelial layer over the dissected surfaces of the aorta sometimes results in a true functioning double aorta.[1]

It is obvious that the clinical course of dissecting aneurysm may closely resemble, and at times may be identical with, that of coronary thrombosis. The following are the main differences:

1. Whereas the onset of pain in dissecting aneurysm is usually sudden, the development of pain in coronary thrombosis is usually gradual and is often preceded by angina pectoris. In a smaller group thrombosis is preceded by attacks of pain of longer duration. The location of the pain of dissecting aneurysm is usually low substernal or in the mid-thoracic back. The pain does not radiate into the arm, except in rare instances, but is apt subsequently to travel, with the dissection, downward into the abdomen. The pain of coronary thrombosis, on the other hand, is not always midpain and usually radiates to the shoulders, arms, hands and other distant areas.

2. The chief characteristic features of the clinical course of dissecting aneurysm are compression of arterial and venous vessels, secondary manifestations of ischemia and hematoma of the aorta. These symptoms and signs often change from time to time. The vascular signs are apt eventually to become more extensive, but in rare instances they clear up as a result of rerupture of the dissection into the main aortic channel, causing partial or complete re-establishment of the circulation.

3. Maintenance of high blood pressure occurs more frequently in dissecting aneurysm than in coronary thrombosis.

4. Aortic diastolic murmurs develop in dissecting aneurysm, but not in coronary thrombosis.

5. Pericardial friction rub is common in coronary thrombosis but relatively rare in dissecting aneurysm. In the latter condition the friction rub usually indicates beginning rupture of the dissection into the pericardial cavity, and therefore it is heard shortly before the onset of pericardial tamponade and death. Hence pericardial friction rub with relatively good peripheral circulation is distinctly in favor of coronary thrombosis.

6. Electrocardiographic changes with characteristic features of anterior or posterior infarction favor the diagnosis of coronary thrombosis.

7. Whereas the majority of patients survive attacks of coronary thrombosis, patients usually succumb to dissecting aneurysm of the aorta.

It is particularly fortunate that in both cases here reported electrocardiograms were obtained before as well as after the onset of the dissection. Until recently, few such observations were available on cases of dissecting aneurysm, and it has been generally held that the electrocardiogram is usually normal. Recently, Glendy and his associates[3] reported a case with electrocardiographic changes in Leads 2 and 3, which were suggestive of cardiac infarction of the posterior or diaphragmatic type. Postmortem examination in this case did not reveal myocardial infarction. The aortic dissection was found to extend proximally to the opening of the right coronary artery. Among the 11 cases observed in the past three years, electrocardiographic changes have been noted in at least 3 cases, in addition to those reported here. In these the dissection extended eventually into the pericardial cavity. The electrocardiographic changes are explained on the basis of cardiac anoxia, secondary to cardiac tamponade, to shock and to acute hemorrhage. The possibility of a certain degree of compression of the coronary arteries during life cannot be ruled out in these cases. The findings in Case 1 above indicate, however, that compression of the coronary artery as a secondary complication of dissecting aneurysm can in rare instances cause myocardial infarction. Hence electrocardiographic changes and coronary occlusion may be part of the picture.

It has been stated elsewhere that radiation of pain into the arm is rare in dissecting aneurysm. An analysis of 10 cases previously reported, as well as

of a larger group in the literature, failed to reveal such radiation without local dissection of the brachial artery.[2] Of 11 subsequent cases observed in the Boston City Hospital from 1935 to 1937, inclusive, there was only 1 in which radiation of pain occurred. This patient, a sixty-two-year-old man, had had attacks of precordial pain for two months prior to the onset of the dissecting aneurysm, which was characterized by aching pain in the chest, later radiating down both arms, into the penis and finally into both legs. The patient showed signs of vascular compression. The clinical diagnosis was dissecting aneurysm of the aorta with occlusion of the mesenteric, renal and iliac arteries. Postmortem examination confirmed the diagnosis of dissecting aneurysm. In addition, aortic stenosis caused by arteriosclerotic changes was found. It is possible that after the onset of dissection the presence of aortic stenosis interfered with the coronary flow, and that this was responsible for the character of the pain. Patients with aortic stenosis may have angina pectoris without coronary disease.

The features of Case 2 are even more unusual, and are of greater significance. The simultaneous occurrence of syphilitic and dissecting aneurysms seems to shatter the clinical axiom that syphilitic aneurysm speaks against the presence of dissecting aneurysm. The facts, however, that histologic examination revealed that the syphilis of the aorta was localized over the area involved by the old aneurysm, and that, contrariwise, syphilis was not present over the area of acute rupture, indicate that we are dealing with a rare case in which the two conditions coexisted. Hence, as in other cases, the acute rupture depended on arterial hypertension and on arteriosclerotic degeneration. Indeed, that the syphilitic inflammation induced a special resistance against the dissection is well demonstrated by the following facts: the dissection did not appreciably invade the old syphilitic aneurysmal wall, whereas it completely dissected the surrounding nonsyphilitic portion of the aorta; and in spite of the thinness of the old syphilitic aneurysm the dissecting aneurysm did not rupture over this area. This case therefore constitutes important direct evidence confirming our belief that the presence of syphilitic aortitis makes dissection difficult. Among the 300 cases of dissecting aneurysm analyzed by Shennan,[1] mainly collected from the literature, there were several in which the presence of syphilis was mentioned. The evidence for syphilis in these cases, however, as is also stressed by Shennan, is insufficient. None of these cases had features similar to those of Case 2.

SUMMARY

1. Two cases of dissecting aneurysm of the aorta with unusual features are described, and reference is made to other cases which have been studied. In the first case, with electrocardiographic changes the dissection invaded the root of the aorta as well as the first portion of the left coronary artery, compressing the lumen of the mouth of this artery. This ischemia resulted in acute myocardial infarction. In the second case the patient suffered from arterial hypertension and from syphilis, and an old syphilitic aneurysm of the arch of the aorta coexisted with acute dissecting aneurysm originating near the opening of the syphilitic aneurysm. Histologic examination indicated that the syphilitic involvement was localized over the chronic aneurysm, while the area involved by the acute rupture contained an atheromatous softening without syphilitic changes. It is concluded that the two conditions occurred independently. The fact that the dissection invaded the syphilitic aneurysm but slightly, whereas it completely ripped the surrounding nonsyphilitic wall of the aorta, confirms the belief that a syphilitic process, through fusion of the layers of the aorta, tends to prevent dissection.

2. Among 2202 necropsies in the Boston City Hospital from 1935 to 1937, inclusive, dissecting aneurysm occurred in 11 instances, a ratio of 1:200. The condition was correctly diagnosed clinically in 7 of the 11 cases. Whereas but 6 cases had been recognized clinically up to 1935, the total number of correctly diagnosed cases now available from the literature is at least 21.

3. The differential diagnostic features of dissecting aneurysm and coronary thrombosis are discussed. Electrocardiographic changes may occur in dissecting aneurysm as a result of ischemia of the heart, due to acute blood loss, shock and pericardial tamponade, or, rarely, as a result of compression of the coronary artery.

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A CHALLENGE TO MEDICINE

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RECENT social changes have been more numerous and radical than at any time in history. Among these developments are many new forms of medical practice which are a striking departure from the time-tested private practice of medicine. On many sides there appear reformers who urge even more drastic changes in the methods of distributing medical care, based on the pattern of foreign systems of sickness insurance. Thus far the medical profession in the United States has averted the entanglements, political domination and inevitable deterioration of medical service that would come from a system of compulsory sickness insurance.

The persistent propaganda of the proponents of socialized medical service has caused many physicians to doubt the future of medicine. A few are even exhibiting a fatalistic attitude in declaring that the socialization of medicine is inevitable.

Unfortunately, not many of those who write or speak in favor of socialized medicine clearly define the term. What is meant by it? Certainly not public health, for that phase of medicine has long been supported by taxation; certainly not the medical care of the indigent, for that is held to be a responsibility of local communities, to be paid for from tax funds; certainly not the institutional care of the mentally sick, the epileptic and the feeble-minded, for present methods appear to be the most appropriate for persons thus afflicted; certainly not the sanatorium management of tuberculosis, for this method has contributed much to the control of that disease; certainly not the medical practice actually required in the clinical phase of medical education, for this is a necessity in the training of physicians; certainly not workmen's compensation, for that system is now provided by statute and is state-supervised to varying degrees. The socialization of medicine, as the term is commonly used, refers to any form of medical advice, diagnosis and treatment provided, conducted, controlled or subsidized by the Federal or any state government, with the exceptions stated.

There are many views as to the type and extent of the social change proposed. There are those who advocate that all medical care should be provided through taxation; that is, physicians should be state employees. Others urge some form of sickness insurance — voluntary or compulsory.

Voluntary sickness-insurance systems are usually the precursors of compulsory systems. No country has ever operated a system of complete state medicine in which all medical services were furnished by physicians who derived their sole income from the state, but many countries have adopted some system of sickness insurance. All these systems may be included in the term "state-managed medicine." No value can be derived from criticism of a country for having adopted a system of state-managed medicine, but a critical analysis of the systems themselves may be helpful in determining whether such methods are preferable to the free and independent practice of medicine such as exists in the United States.

A careful examination of the systems of state-managed medicine reveals the following conditions:

1. There is no decrease in the cost of medical care. Instead, the system adds a staggering cost of administration.
2. Public health and preventive medicine are not assisted or advanced. State-managed medicine does not provide the annual health examinations or the immunizations usually promised before the system was adopted.
3. Morbidity and mortality are not reduced.
4. The problem of so-called catastrophic diseases is not solved.
5. Neuroses are created.
6. Overmedication is encouraged.
7. The burden of the system is distributed over the low-income class, which is least able to bear it.
8. Medical care for the indigent is omitted.
9. The medical profession is divided into a "first" and a "second" class.
10. Graduate education is not encouraged and is usually neglected.
11. The hospital load is increased. Hospitals are encouraged to practice medicine.
12. Attention and financing are concentrated on the less essential health and medical measures.
13. Diagnosis and treatment are mechanical and superficial.
14. Professional associations are compelled to devote their energies to the defense of medicine against non-medical and political interference rather than to scientific and educational activities.
15. Medical service becomes a political issue.
16. Control over medical service is placed in the hands of unqualified, non-medical individuals and organizations.
17. The road is closed to the use of more desirable methods.

Some European medical observers are now bolder than formerly in criticizing their systems of state-managed medicine. They are saying that sickness

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is not definitely or exclusively an insurance risk, but had to be forced into this position by insurance. They admit that sickness insurance establishes a bureaucratic, organized, wholesale business in human misery, with central control and many branch establishments. They assert that social insurance is built on compulsion and on compensation against hazards; but compulsion leads to distrust, and regulation of risks leads to greed. Compulsion was necessary because only in this way was it possible to include broad sections of the population which were presumed to be in need of medical care but would not enter the system unless compelled to do so.

They have observed that sickness insurance has constantly restricted the direct relations between patients and physicians in private practice. Formerly there was a human relation which depended on confidence in the physician. Between the patient and his physician there is now a third party — the insurance carrier — and a fourth party, — the government, — a supervising bureaucracy which compels the physician to follow its regulations. Furthermore, these observers assert that if treatment does not bring the expected result, the physician is discredited and is made punishable for every unavoidable failure.

Reports from countries having state-managed medicine state that the insured have not been satisfied with the new system. Restrictions of the means of healing have been offensive to them; they have looked on the contributions to the sickness-insurance system, taken from them through their employers by compulsion, as a retained share of their wages. They knew that they could obtain this retained money only in the form of insurance medical service or cash benefits; they believed they had been compelled to pay out money without receiving an equivalent; the only way in which the money or an equivalent could be recovered was to declare themselves sick and to meet the conditions set down by the law; this was an easy matter.

The reports continue with a criticism of the action of political parties which are using sickness insurance as the first step in the governmentalizing of all health care for the entire population. This point has not been reached, but it appears to be the objective.

Even in Europe some physicians have expressed the view that the idea of a free medical profession must not be abandoned; once it is completely abolished a cultural value will have been lost that cannot be replaced or restored. To physicians, human values are of greater importance than are political expedients.

These are only a few of the characteristics of systems of state-managed medicine. All such systems are not subject to the same criticisms, and those in some countries have been greatly improved since their inception by the continuous efforts of the medical profession of those countries.

Even at its best, do the American people and the American physicians want such a system? Before we wholly destroy our present plan of medical practice through revolutionary legislation, let us inquire carefully into the value of what we have, and study searchingly the proposals of those who would take it from us, lest worse come in its place.

If there is truly any lack of good medical service for those who require it, the medical profession stands ready now, as it has invariably stood in the past, to supply that service. What other profession has ever developed such a tradition of sacrifice for the public welfare? It has been said that the rich and the poor get the best of medical care, and that the members of the great middle class suffer because they are unable to pay the costs of modern medical service.

The proponents and agitators for some radical change in the method of distributing medical services have made some serious and startling charges concerning the methods now in use. They continue to assert that 50 per cent of the population receives no medical care. A survey of some 38,600 persons made by the Committee on the Costs of Medical Care showed that 47.1 per cent had no illness over a period of more than a year. The study also showed that 47.9 per cent of these persons had the services of physicians. Only 5 per cent of the persons involved in the survey were presumably in need of medical services but for some reason did not avail themselves of medical care. Perhaps 5 per cent is not too large an estimate of those who because of human characteristics manifested as ignorance, stupidity or prejudice prefer cultism, patent medicines, the advice of friends or relatives or no medical service at all.

The medical profession today is conducting more social experiments in the methods of distributing medical services than all of the proponents for change have ever conducted. Out of the two hundred or more projects that are being studied or operated by county or state medical societies, it is hoped that methods may be found that can be utilized to supplement existing medical facilities wherever necessity demands.

These proponents and agitators have charged that the medical profession is static and obstructive. But without any compulsion from political or governmental sources, the profession has sought constantly to advance the standards of medical education, medical licensure and hospital practice, and is now making notable progress in the certifica-

tion of specialists. To a remarkable degree these objectives are being accomplished. Today both curative medicine and preventive medicine have advanced to new and higher planes of efficiency. The profession is constantly perfecting methods of diagnosis and treatment; there has been a striking reduction in the prevalence of certain communicable and infectious diseases; infant mortality has been greatly reduced; and in the past century life expectancy at birth has been increased from twenty-eight years to almost sixty.

These meddlers with medical practice assert that present methods in the United States are costly and inefficient. In countries having state-managed medicine, there are as many bureaucratic employees as there are physicians giving medical service. State-managed medicine imposes such extensive red-tape, record-keeping and political interference, dominance and control on the physicians practicing under the system that they cannot devote the time they should to the actual practice of medicine. Loading the system with unnecessary bureaucratic personnel and with political meddling and direction tend to increase the cost of medical service and at the same time to reduce its quality.

It is claimed by the supporters of social reform in medicine that state-managed medicine will raise the standards of medical practice, deal a death blow to cultism and quackery and encourage preventive medicine and immunization. Standards of medical practice have advanced faster in the United States with free and independent medical practice than in any country having state-managed medicine. Germany, after fifty-four years of sickness insurance, is the happy hunting ground for quacks. It is the only nation to give official recognition and endorsement to all forms of quackery. Preventive medicine in the United States is the envy of the medical profession in many foreign nations.

The medical profession has always been its own most severe critic, and notwithstanding the advances that have been made toward a better understanding of disease and its control, it recognizes that there are some conditions and practices that should be corrected. For example, there are areas in which there seems to be an uneven distribution of physicians and other medical facilities, and in which the evils of contract and corporation practice should be corrected, the alleged abuse of clinic and hospital facilities should be investigated, the unwarranted practice of medicine by boards of health and boards of education eliminated, the medical phase of workmen's compensation improved and the dangers in group hospitalization recognized and averted.

In all these and many other problems confronting medicine, there are both ethical and economic dilemmas. The fundamental concept in both ethics and economics is that of value. In economics the ultimate test of value is the amount of goods which will be consumed or the medium of exchange which will be paid in the market. Ethics embraces a wider conception, and makes as its ultimate test of value the effect on the individual and on the society in which he lives. Medical ethics deals with direct individual and personal services between whole personalities. Medical relations cannot exist between an oculist and an eye, a corporation and a broken law, a hospital and a disease, a laboratory and a blood specimen or an insurance policy and a compensation case. If medical relations are to be ethical — that is, in furtherance of the ultimate good health of the patient — they must be between the patient who is to be treated and the physician, trained according to established standards and having access to the accumulated knowledge of the ages.

To combat the agitation for drastic changes in medicine, the medical profession must continue to practice good medicine. It has been accused of being individualistic. This criticism should be accepted as a compliment insofar as the diagnosis, treatment and close personal confidential relations of private practice are concerned. Physicians must continue to be individualistic and ethical in their private ministrations to maintain health and to alleviate sickness. But they must speak and act collectively on matters pertaining to economics, public relations, legislation, the preservation of professional ideals and traditions, and the maintenance and advancement of medical ethics and the standards of medical education and practice.

There is within the medical profession in the United States a small but loudly vocal minority which would hasten the advent of some form of state-managed medicine, with all its methods of mass production, assembly-line technic and political dominance and control. These few physicians do not speak for the vast majority of substantial and representative physicians who cherish the free and independent practice of ethical medicine. This noisy minority does, however, appeal to and has the support of a group of non-medical propagandists and agitators who see in a system of state-managed medicine an opportunity for position, power and plunder. A few physicians whose acts and statements are filled with scorn, ridicule and derision for the ideals, traditions and ethics of medicine must not be permitted to speak for reputable and substantial physicians who believe in the institution of ethical medicine.

Quacks are abroad plying their trade in the realms of economics, sociology and ethics as well as in the field of medicine. Large groups of people

under the stimulation and leadership of these extremists and self-styled experts are assuming to know that which they do not know. They are contemptuous of the experiences of the past; they decry special skill; they substitute rhetoric for reason. The large and representative group of ethical physicians have an obligation to unite solidly in sentiment and in action against the utterly false representations of the reactionary, radical, self-styled experts who would destroy medical values that have required generations and centuries of accumulated scientific effort and experience to acquire.

The medical profession has not discharged its entire obligation to society by healing the sick or preventing disease. Its broader obligation lies in a concerted determination and effort to preserve that form of practice which best conforms to good public policy and which will perpetuate the free, independent, scientific and ethical institution of medicine.

The important question is this:

Shall medicine continue to be practiced by men and women who are scientifically trained and who are devoted to the relief of suffering humanity, or shall the practice of medicine be taken over by a group of medically untrained bureaucrats who will use the medical profession as a tool and the sick as clay in moulding a huge political machine?

The obligation of the medical profession seems clearly defined. It must vigorously resist all efforts that are likely to provide sick people with the mere dregs of medical service, or that are destined to reduce medicine to the serfdom of science.

Now that the economic phase of medical practice is demanding more consideration, ethical relations must not be forgotten or removed from the central position they have always held. On the contrary, economic relations and plans, just as much as professional services and conduct, must be tested by the principles of medical ethics. Medical ethics is not outgrown or antequated; it must continue to be vital, elevating, dominating and enduring through continual respect and adherence.

When physicians become, if they ever should, mere robots, making diagnoses from card indexes and mechanical gadgets and prescribing treatment from prepared and numbered labels, and when patients become a mere collection of interesting human parts to be shunted from one corner to another of a medical repair shop for some heartless and pseudoscientific tinkering, America will have lost one of its greatest institutions, — free and independent medicine, — and the American people will have lost some of their most valuable human traits, namely confidence in, respect for, and reliance on the scientific men and women who protect their health and prolong their lives.

PRIMARY THROMBOSIS OF THE AXILLARY VEIN

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THROMBOSIS of the axillary vein following strain (effort) has been comprehensively described by Matas.[1] Primary or idiopathic thrombosis occurring spontaneously is rare. We report below a case in which no etiology could be found and in which studies by means of an opaque medium visualized the obstruction.

CASE RECORD

C. F. M., aged 32, married, was admitted to the Boston City Hospital on May 4, 1935. Two weeks before admission he had had an upper respiratory infection accompanied by a slight cough, which cleared up in the course of a week. He was not incapacitated and aside from a healing herpes simplex on his upper lip there were no residual effects. Five days prior to admission the patient felt some discomfort in the left shoulder. There was, however, no spontaneous pain or pain on motion, and no areas of tenderness were present. This condition persisted for about 3 days. Two days before entry the patient noted that his left upper extremity felt heavier and appeared larger than his right. He reported to the Outpatient Department of the Boston City Hospital, where the condition was diagnosed as venous thrombosis. X-ray photographs were taken, and the patient was sent home to rest. He was seen at home by one of us (J. A. F.), who sent him to the hospital.

His past history was important only in that he had indulged in alcohol quite freely at times. The family history was noncontributory. The patient was an electrician's helper by occupation. He was right-handed.

Physical examination showed a robust young man whose general condition was entirely normal except for the findings revolving around his complaint. The neck showed no adenopathy, the thyroid gland was not palpable, and there were no abnormal pulsations. The lungs were clear and resonant throughout; there were no rales or abnormal breath sounds. The heart showed no murmurs or thrills, and the rhythm was regular. There was no displacement of the cardiac dullness. The lower extremities showed no varicosities.

The left upper extremity was larger in circumference than the right, and the skin was colder and darker. There was a definite increase in the number of visible superficial

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veins, and the veins were much more prominent than in the right extremity. Palpation of the left axillary vein was accompanied by a slight degree of tenderness. The vein presented a typical cord-like tumefaction. There were no changes in the reflexes, and no motor or sensory changes. The radial, brachial and axillary arteries were easily palpable. On the anterior thoracic wall many dilated venules were visible, and the skin of the upper half of the thorax anteriorly on the left side seemed slightly darker than the skin elsewhere.

The laboratory findings were as follows. The urine had a specific gravity of 1.027, with no albumin and no sugar;

Figure 1.

the sediment was negative. The hemoglobin was 74 per cent. The red-cell count was 4,500,000, and the white-cell count was 8000, with 68 per cent polymorphonuclears, 21 per cent lymphocytes, 5 per cent monocytes, 3 per cent eosinophils and 3 per cent basophils. The blood Kahn test was negative, and the nonprotein nitrogen was 27 mg. per cent. A blood culture showed no growth.

A tentative diagnosis was made of thrombosis of the axillary vein, with a suspected mediastinal mass on the left side or possibly a cervical rib.

Visualization of the vein was undertaken in order to rule out the possibility of pressure by an obscure mass, to locate the site of obstruction, to note changes in the contour of the distal portions of the vein, and to observe the nature of the collateral channels. For outlining the course of the vein we first used Skiodan. The injection was carried out in the x-ray department and the films were taken during the injection. The injection, which was done about 2 weeks after the onset of the symptoms, was reported as follows: "Examination of the left upper arm after the injection of Skiodan [Fig. 1] in the antecubital vein shows a portion of the brachial and the axillary vein outlined. The brachial vein is considerably narrowed and one of the valves is markedly dilated. The collateral branches cannot be traced. These findings are consistent with thrombosis of the brachial and axillary veins." An infrared photograph taken at this time demonstrated the venous collaterals in the arm and chest (Fig. 2).*

Following his discharge from the hospital, this patient resumed his occupation and has worked without interruption. He has never noted any swelling or pain, or

Figure 2.

indeed any symptoms referable to his arm. Subsequent examinations showed no special prominence of the veins on the left upper or lower arm as compared with those on the right. Tests for hydrostatic effects were negative, and measurements revealed no material difference.

This patient was last seen 14 months after leaving the hospital. On this occasion he reported that he was still free from symptoms. The examination of the extremity and a general physical examination were both negative, so that on the basis of clinical findings there was nothing to indicate any alteration in the circulatory function of the affected arm. At this time an x-ray film (Fig. 3) taken after the injection of 10 cc. of Hippuran showed the entire axillary vein well outlined, its caliber slightly larger and some of the branches partially outlined. One of the branches of the axillary vein could be traced. The valves were not so dilated as they had been at the previous examination. There were no changes in the humerus or in the surrounding soft tissue.

In general, cases of axillary thrombosis fall into one of three groups. The first comprises those sec-

*We are indebted to Dr. Edward A. Edwards for the infrared photograph.

ondary to intravascular or extravascular inflammatory processes or extravascular pressure from contiguous neoplasms or enlarged nodes. The second group comprises cases resulting from a sudden strain or other trauma. In the third group are included a small proportion of cases which in the absence of any known trauma must be classified as idiopathic; yet in these it is impos-

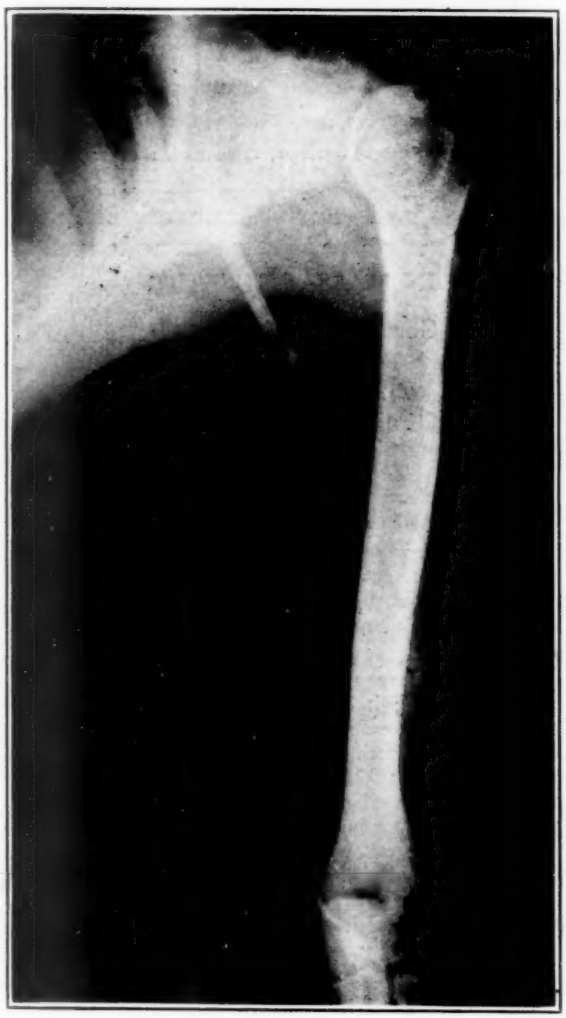

Figure 3.

sible to rule out trivial trauma or, as Matas terms it, "banal" trauma. The second and third groups are characterized by the sudden development of edema, pain in the affected extremity, varying degrees of cyanosis, and a palpable cord-like mass, often tender, representing the axillary vein.

The literature concerning axillary thrombosis caused by strain was adequately reviewed by Matas[1] in 1934. Paggi's[2] survey resulted in the collection of only 74 reported cases up to July, 1933. Despite this apparent paucity, the impression prevails that many cases have never been reported. This applies particularly to the American literature. Cases of primary thrombosis of the idiopathic type have proved even rarer.

The mechanism of the development of the condition remains obscure, and many theories have been developed to account for it. Von Schrötter,[3] who reported the first case, regarded it as a localized phlebitis resulting from the sudden traumatic stretching and compression of the vein. Subsequent studies led to the theory that the trauma occurred between the clavicle and the first rib, with the costocoracoid ligament and the subclavius muscle as contributing factors. Slowing of the circulation, rupture of the subclavioaxillary valve, venospasm induced by sympathetic irritation of traumatic origin, a tear in the wall of the vein—these and several other factors have been invoked. The reader is referred to the exhaustive articles by Matas[1] and Veal and McFetridge[4] for a complete discussion of this subject. The lack of autopsy material has proved a distinct handicap in determining the pathogenesis.

Veal and McFetridge[4] studied the problem both in the living subject and in fresh autopsy material. They report 2 cases of primary thrombosis. They approached the subject by vasographic studies on normal subjects, using Thorotrast (colloidal thorium dioxide) as the opaque medium. They noted that anatomical relations changed when the factor of movement was introduced; the axillary vein was capable of accommodating itself to moderate changes in position. On hyperabduction and external rotation, there was a compression of the vein as the subscapularis muscle came to lie between the vein and the head of the humerus. They determined that the obstruction occurred at the point where the vein passed over the subscapularis muscle in the position of hyperabduction and external rotation. In this position the emptying time was shorter rather than longer. Additional observations demonstrated that the important factor in raising the venous pressure is not the position of the arm, but rather the increased thoracic pressure which is caused by coughing or straining.

COMMENT

The absence of an etiologic background has forced us to assume that the case herein reported belongs to the rare group of idiopathic or primary axillary thrombosis. The patient was known to have indulged freely in alcohol, but no alcoholic bout preceded the onset. It is doubtful whether alcoholism per se plays any role other than through

the traumatism that may accompany it. We have admitted annually to our service approximately 850 patients with acute alcoholism, some in a severely toxic state. The rarity of axillary thrombosis among these individuals goes to prove that alcoholism plays no direct part in the etiology of this disease.

Along with the distinctive characteristics typifying the condition in our case, there were several atypical features. The onset was gradual, and was unaccompanied by pain. The edema was also relatively slow in development. There was only slight tenderness on palpation of the vein. The patient was right-handed, and the left axillary vein was the seat of thrombosis.

SUMMARY

An additional case of primary thrombosis of the axillary vein is reported. We have placed this in the idiopathic group because of the absence of trauma or any other inciting cause. Vasography revealed the site of the thrombosis. A follow-up vasogram taken fourteen months later still showed some radiographic deviation from the normal.

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REPORT OF TWO CASES OF BOTULISM IN MASSACHUSETTS

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BOSTON

DURING the period 1899-1935, botulism has been reported only six times in the New England States.[1] Only once in the United States has it been reported as being acquired through the ingestion of home-canned mushrooms. It is of interest, therefore, to report 2 such cases which occurred recently in Cambridge.

Case 1. C. P., a 48-year-old man, on January 16, 1937, ate some wild mushrooms which had been picked 6 months before in the woods of a near-by suburb and canned at home. Previously, the home-canned mushrooms had always been reheated before being served. This time, however, they were not. No effect was noted that day or the next, when the man again ate a jarful of these mushrooms, unheated. On January 18 he arose with a dizzy headache, and was nauseated and unable to see distinctly. He went to work, but soon returned home because of his inability to see what he was doing. There was no vomiting, and he had no bowel movement that day. His tongue felt stiff, he could not swallow well, his speech became thick, and he then began to see double. At this point he was sent to the Cambridge Hospital by Dr. J. P. Nelligan, of Cambridge, with whose permission these cases are presented.

Physical examination revealed a well-developed and well-nourished adult male, rational and co-operative but slightly drowsy, and complaining of blackness before his eyes. The temperature was 97.2°F., the pulse 60 and the respirations 20. The blood pressure was 110/70. Paralysis of all the ocular muscles was present. Print could not be read, the patient stating that he saw double. The optic disks were pale. The face was slightly puffed out on the right side. The tongue and jaw were deviated to the right. The palatal reflex was absent. The speech was thick and slurring and the enunciation of words was impaired. There was difficulty in swallowing, with regurgitation of fluids through the nose. The breath was foul. There was no stiff neck. Generalized muscular weakness was present. Tendon reflexes were exaggerated. The abdominal reflexes were absent; the Babinski response was present bilaterally, but there was no Kernig or clonus.

The patient grew worse while on the ward; he was totally unable to swallow, choking and gagging when taking fluid and regurgitating it through the nose. The speech became mumbling. His mind remained clear at all times.

The urine gave an acid reaction and had a specific gravity of 1.026; it contained no sugar or albumin but showed a 2+ acetone reaction; the sediment was negative. The white-cell count of the blood was 5100, and the red-cell count 3,280,000. The hemoglobin was 62 per cent (Sahli). A blood Hinton test was negative. The spinal fluid had an initial pressure equivalent to 170 mm. of water; dynamics were normal. The fluid was clear and colorless and no cells were found; the total protein was 29 mg. and the sugar 77 mg. per 100 cc.

A clinical diagnosis of botulism was made; botulinus antitoxin was sought, but could not be obtained until the following morning. In the meantime 1/4 gr. of morphine was given every 4 hours, and a hypodermoclysis of 1500 cc. normal saline and 5 per cent glucose was administered. Then 20,000 units of a polyvalent botulinus antitoxin (Lederle — labeled "for use in animals") was given intravenously at regular intervals over a 12-hour period, the patient first being tested for serum sensitivity. He was then transferred to the Boston City Hospital and placed in a respirator because of beginning respiratory distress. However, this complication cleared within 1 day. At that hospital he received an additional 115,000 units of the polyvalent antitoxin in divided doses at regular intervals. Clyses and intravenous solutions of 3000 cc. of fluid were given daily. Serum sickness developed a week later and soon cleared up. The paresis of the larynx and pharynx continued until the 12th day after entry, when the patient began to swallow small amounts of fluid. From then on he took his own nourishment. The cranial nerve palsies subsided. He slowly regained

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strength and at the time of discharge it had returned to a remarkable degree, although there was considerable generalized wasting of subcutaneous tissue. On February 13, or 26 days after the onset of the disease, he was discharged improved.

When seen 9 months later, he had completely recovered.

Case 2. M. P., aged 43, the wife of the patient in Case 1, was admitted to the Cambridge Hospital on January 20, 1937, with a history of nausea, difficulty in swallowing, weakness and blurred vision of 1 day's duration.

Four days before entry she ate a small amount of the above-mentioned home-canned mushrooms which had not been reheated. She was well for 3 days, or until January 19, when she began to feel nauseated, became weak, and developed progressive difficulty in swallowing and blurring of vision. She was then sent to the hospital.

On admission the temperature was 97°F., the pulse 115, and the respirations 20. The blood pressure was 160/100. Physical examination revealed a flushed face, unsteady gait and nasal speech. The patient continually cleared her throat in an attempt to get rid of the mucus. There was a right-sided facial palsy of peripheral type. She was unable to read print because of blurred vision. The eyes showed a partial paralysis of all the extrinsic ocular muscles. Both optic disks were pale. The breath was foul; the tongue was coated and deviated to the right. The palatal reflex was absent. There was a marked inability to swallow, and attempts to take fluid caused gagging and choking. The neck was slightly rigid. The heart and lungs were negative. There was marked weakness of the arms and legs. Abdominal reflexes were absent on the left, and a Babinski response was present on the left, but there was no clonus or Kernig.

On January 20, the urine showed an acid reaction and a specific gravity of 1.016. There were no sugar and no albumin, but a heavy trace of acetone. The sediment was negative. The white-cell count of the blood was 14,000, with 85 per cent polymorphonuclears, 12 per cent lymphocytes and 3 per cent monocytes. The red-cell count was 4,500,000, and the hemoglobin 85 per cent (Sahli).

The patient could take nothing by mouth for the next 3 days, and received 3000 cc. of fluids intravenously and by clysis each day. A total of 50,000 units of polyvalent botulinus antitoxin was administered in the following doses: 5000 units in divided amounts was given in the 1st hour intravenously; the next morning 25,000 units was given with the clyses and intravenous infusions; that afternoon 5000 units was given intramuscularly; the third day 10,000 units was given with the clyses; and on the 4th day, when definite improvement had been noticed, only 5000 units was given with the clyses.

By that time the patient's vision had improved to the extent that she could read print, the nasal tone of the voice was markedly lessened, and she no longer kept clearing her throat. Her eye condition remained about the same, but the palatal reflex returned, and she was able to swallow small amounts of fluid without choking or regurgitating through the nose. The Babinski response became equivocal.

From then on she steadily improved, except for a serum reaction which developed on January 27, and was successfully treated by adrenalin and magnesium sulfate and calcium lactate by mouth. Her weakness gradually disappeared, and the gait soon improved and became normal. On discharge, February 6, or 18 days after admission, she showed only a very slight residual weakness of the eye muscles.

The patient was completely recovered 9 months later.

Attempts to prove the presence of the botulinus bacillus or its toxin were unsuccessful. Unfortunately there was no sample of the unheated mushrooms of the first jar from which both patients had been served. Some mushrooms from another jar were found in a garbage can on January 21. These and an unopened jar were sent to the Bacteriology Department of the Tufts College Medical School, and also to the Antitoxin and Vaccine Laboratory of the Massachusetts Department of Public Health. Cultural and animal inoculation tests were negative for *Clostridium botulinum* or its toxins; hence only a clinical diagnosis of botulism could be made.

DISCUSSION

The early recognition of botulism is very important, so that antitoxin may be administered promptly. Botulism is an acute poisoning caused by the toxin of *Clostridium botulinum*.[2] The bacillus is essentially a soil organism and is found in dust, dirt, carrion, fruit, vegetables and plants. Under anaerobic conditions the growing bacillus produces a thermolabile poisonous toxin, which when ingested affects primarily the cells of the central nervous system. Mushrooms, the food ingested in these cases, have only once been reported as the carrier of the bacillus or its toxin. Botulism should be seriously considered in every case of poisoning caused by the ingestion of canned mushrooms.

The incubation period usually varies from eighteen to thirty-six hours after ingestion of the toxin, but symptoms may occur as early as two hours and as late as eight days after.[3] The period was forty-eight hours in Case 1 and seventy-two hours in Case 2. Early constipation, an outstanding symptom of botulism, was present in both patients. Disturbance of vision was caused by paresis of the ocular muscles, and was a prominent symptom. Fatigue, with vertigo and headache, was soon followed by generalized muscular weakness, this being the usual course of the disease. Loss of the light reflex, which may or may not occur, was not present. Within a short time there was a

Table 1. *Signs and Symptoms of Botulism.*

REPORTED SIGNS AND SYMPTOMS	CASE 1	CASE 2
Constipation	+	+
Fatigue, with vertigo and headache	+	+
Paresis of ocular muscles, producing disturbance of vision	+	+
Loss of light reflex	—	—
Paresis of pharyngeal and lingual muscles, producing dysphagia and dysphonia	+	+
Generalized muscular weakness	+	+
Absence of sensory disturbances	+	+
Subnormal temperature	+	+
Slow pulse	+	—
Disturbance of respiration	+	—
Mental alertness	+	+
Absence of vomiting and diarrhea	+	+

paresis of the pharyngeal and lingual muscles, producing difficulty in swallowing with regurgitation through the nose, and difficulty in talking. This group of symptoms is very common in botulism. The absence of sensory disturbances, diarrhea and vomiting, and the presence of mental alertness, subnormal temperature and a slow pulse in our patients corresponded unusually well with the textbook description of the disease.

The duration of the disease varies from two to twenty-six days. When recovery occurs, convalescence is slow and tedious. Disturbance of vision is usually the last symptom to disappear, and may persist for months. There seems to be no permanent severe disability after recovery. Where death occurs, it is usually caused by a terminal bronchopneumonia or by respiratory paralysis.

The differential diagnosis includes mushroom poisoning, bulbar poliomyelitis, encephalitis and food infection. Mushroom poisoning had to be ruled out first in these cases. In botulism the incubation period is long, because the bacillus produces a toxin which mediates its symptoms through the central nervous system, while in mushroom poisoning the period is much shorter, the poison directly affecting the gastrointestinal tract, with subsequent vomiting, diarrhea and abdominal cramps. The latter poison may also produce nephritis with anuria or hemoglobinuria, mental confusion, excitement and convulsions, and excessive perspiration and lacrimation. Bulbar poliomyelitis and encephalitis were seriously considered, but in view of the fact that the spinal fluid findings were entirely negative, they also were ruled out. Food infection (so-called ptomaine poisoning) was ruled out by the absence of gastrointestinal symptoms such as vomiting, diarrhea and abdominal cramps, by the absence of fever, and by the presence of marked disturbance in the central nervous system.

Meyer[1] quotes Velikanoff[4] as showing that in a series of 194 Russians poisoned by botulinus toxin 119 were treated with antitoxin and 24, or 20 per cent of those treated, died. Seventy of the 75 untreated cases died, a mortality of 93 per cent. In the experience of the Russian observers, one may expect a reduction in the mortality of botulism provided the antitoxin is administered within the first seventy-two hours after ingestion of the botulogenic food. Large doses should be administered early either by intramuscular or intravenous route, the latter being preferable. Case 1 received 135,000 units without harmful effects other than a mild serum reaction.

Supportive treatment consisting of 5 or 10 per cent glucose in normal saline solution by clysis or intravenous route is an important measure. Rosenau[2] states that the patient should be kept under the full influence of morphine until the antitoxin is obtained, for in the experimental disease this opiate delays the action of the toxin. The stomach should be washed out and the bowels purged with an active cathartic. A respirator should be available in case of respiratory failure.

SUMMARY

1. Two cases of botulism, clinically diagnosed and following the ingestion of home-canned mushrooms, are reported. Recovery took place in both cases, polyvalent botulinus antitoxin being administered within seventy-two hours after ingestion of the food, and twenty-four hours after the onset of the symptoms.

2. Only 6 cases of botulism have been reported in New England in the period 1899-1935, and in the same period only 1 case in the United States has been attributed to eating mushrooms.

3. Early recognition of the disease, with prompt administration of the antitoxin, is important in reducing the mortality.

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ANAPHYLAXIS TO SODIUM MORRHUATE FOLLOWING INJECTION TREATMENT OF INTERNAL HEMORRHOIDS

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SINCE the introduction in 1929 of sodium morrhuate as a sclerosing agent, it has attained considerable popularity in the treatment of varicose veins, hydroceles, olecranon and prepatellar bursitides and internal hemorrhoids. The purpose of this paper is to report 2 cases of severe constitutional anaphylactic reactions which have occurred following its use in the injection of internal hemorrhoids. Probably many other such reactions which have taken place have not been reported. They constitute a distinct hazard, and should be guarded against.

In reviewing the literature we find that Cooper[1] in 1933 reported a mild dermatitis with an annoying pruritus following the use of 10 cc. of a 5 per cent sodium morrhuate solution.

Allergic-like reactions to this agent when employed for the obliteration of varicose veins have been reported by Zimmerman[2] and Lewis.[3] Praver and Becker[4] from their dermatologic clinic reported untoward reactions in 7 out of 126 patients who received 783 injections of a 5 per cent solution.

According to Haines,[7] the mechanism of its action is somewhat obscure, and no criteria as to what constitutes sodium morrhuate have been laid down. He states that some commercial samples were analyzed, with a view to ascertaining the degree of uniformity attained by various manufacturers. Examination disclosed considerable differences between the solutions: some were clear at room temperature, while others were turbid or gelatinous or contained a crystalline sediment. The solutions were analyzed for the content of fatty acids and for their iodine value. It was found that sodium oleate is both more toxic and less active as a sclerosing agent than are the sodium salts of the more highly unsaturated fatty acids. The iodine value rises as the elimination of oleic acid from the unsaturated fraction becomes more complete.

Sodium morrhuate is a mixture of the sodium salts of the unsaturated fatty acids occurring in cod-liver oil, and it is thus impossible to give its chemical formula. Originally, the name "morrhuic acid" was given by Gautier and Mourges to a nitrogenous putrefaction product, hydroxydihydropyridine butyric acid ($C_9 H_{13} NO_3$), found in rotted cod-liver oil, but this term is now applied to the product obtained following the hydrolysis of purified cod-liver oil. This impure morrhuic acid is then neutralized with caustic soda, and is further purified by partial fractionization in order to give a sodium morrhuate suitable for medicinal use.

Zimmerman[2] has raised the question whether the saponified fatty acids themselves are capable of producing an allergic reaction, or whether the latter is due to an admixture with liver protein. Another theory which has been offered is that hemolysis may occur, the contact of the patient's blood with the solution resulting in liberation of protein substances which are responsible for the reaction. Still another theory, advanced by Lewis,[3] is that sodium morrhuate may act as a hapten and sensitize susceptible individuals, particularly if they have received an injection one or two weeks before.

I have used a 5 per cent solution of sodium morrhuate in the injection of large internal hemorrhoids in 75 cases. In 2 cases in this series severe constitutional anaphylactic reactions were noted, and are here reported.

Case 1. Mr. W., aged 30, was seen on February 14, 1937, and gave a history of bleeding from the rectum for 3 months. Palpation of the anus and rectum disclosed no new growths, polyps, fissures or fistulas. Proctoscopic examination brought into view a ring of internal hemorrhoids. Sigmoidoscopic examination to a depth of 23 cm. was negative. One cubic centimeter of a 5 per cent solution of sodium morrhuate was injected about the posterior right internal hemorrhoid. The plunger of the syringe was withdrawn before the injection was started in order to make sure that the needle did not enter a vein. No untoward reaction occurred.

One week later 1 cc. of sodium morrhuate was injected, this time into the region of the posterior left internal hemorrhoid. The patient immediately complained of feeling ill and very warm. He also felt dizzy and nauseated. He paled markedly; perspiration became profuse and the respirations shallow; the pulse was imperceptible; and the blood pressure dropped to 60/0. A subcutaneous injection of 1 cc. of a 1:1000 adrenalin solution was given immediately. Spirits of ammonia were also administered. The attack lasted for 20 minutes. After resting for about 1 hour he was allowed to return to his home. He reported that he felt badly for 2 days following the injection. The suddenness and severity of this attack, as well as the danger of immediate death, showed the advisability of using another sclerosing solution for this patient.

Case 2. Miss K., aged 22, was seen on May 10, 1937 and complained of profuse bleeding from the rectum and rectal prolapse. Proctoscopic examination brought into view large internal hemorrhoids which prolapsed on

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withdrawal of the proctoscope; no other lesions were seen. Operation was advised, but was refused in favor of injection treatment. An injection of 1 cc. of 5 per cent solution of sodium morrhuate was made under the mucosa above the internal hemorrhoid in the right lateral anterior quadrant, with care not to inject directly into the vein. The patient was asked to return in 1 week. No reaction except a sensation of fullness in the rectum was experienced. The patient returned in 2 weeks, and was again injected with 1 cc. of 5 per cent solution. Immediately after the injection she complained of nausea, pain in the lower abdomen, a desire to defecate, a feeling of weakness, and dyspnea. The face became pallid; the radial pulse was not felt; the pupils became dilated; and the blood pressure was 64/0. A subcutaneous injection of 1 cc. of a 1:1000 solution of adrenalin was given immediately, and a teaspoonful of spirits of ammonia in water was given by mouth. The attack lasted for 20 minutes, and the patient was allowed to leave the office after resting 1½ hours. She complained of feeling ill for 1 day. The drug was not used at subsequent visits.

DISCUSSION

It is well known that a drug idiosyncrasy may give symptoms identical with those observed in patients sensitive to pollens, foodstuffs or other material containing protein. The 2 cases just reported show that the severe anaphylactic reaction obtained by the use of sodium morrhuate can threaten the life of a patient. If this reaction is allergic, precautions identical with those taken against subcutaneous or intravenous medication with a foreign protein or protein-like substance must be observed in the use of sodium morrhuate as a sclerosing agent, whether for internal hemorrhoids or for any other condition. It might be well in each case to test for sensitivity to sodium morrhuate before using it. A patient may become hypersensitive to the drug if more than from seven to ten days elapse between injections. In this event, immunization should be undertaken with small doses, beginning with 0.2 cc. injected intradermally. To alleviate the extreme anaphylaxis in severe cases, 1 cc. of adrenalin in 1:1000 solution should immediately be given subcutaneously. An ampule of coramine or atropin, gr. 1/150 or 1/75 respectively, should be given hypodermically if there is cardiorespiratory embarrassment. In extreme cases artificial respiration should be resorted to.

SUMMARY

The use of a 5 per cent solution of sodium morrhuate for injections of internal hemorrhoids should be accompanied with the greatest of care in patients who have received previous injections with this solution, as well as in those receiving it for the first time.

Several theories have been advanced as to the causes of anaphylactic reactions from injections of sodium morrhuate.

Two cases of severe anaphylactic reaction are reported.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 24121

PRESENTATION OF CASE

First admission: A thirty-one-year-old, white, steam-shovel operator entered the hospital with the complaint of headaches of ten days' duration.

Ten days before entry he fell on the stairs of a subway station, striking the back of his head. He felt a little dizzy and about an hour later suddenly felt nauseated and vomited. About two hours later he again vomited and developed a severe generalized headache. He was able to sleep that night and went to work the following morning. For the next six days he worked regularly but felt poorly, vomited frequently, and had severe, almost constant headache, neck pain, and low-back pain. Three days before entry he went to bed because of constant nausea. He was unable to eat anything, and the back pain became increasingly more severe. He noticed slight deafness in his left ear and had temperatures ranging from 100 to 101°F.

Twelve years before entry the patient slipped and struck the back of his head. He lost consciousness and remained unconscious in a hospital for seventeen days. The entire right side of his body was paralyzed, but he recovered completely and except for temporary deafness in the right ear remained free of symptoms until two years before entry when he was hit on the head and developed diplopia. Double vision had continued up to entry. His wife and four children were living and well. His past history and family history were otherwise noncontributory. He denied venereal disease.

Physical examination revealed a well-developed and nourished, slightly deaf man complaining of pain in the neck and back which was increased by moving. His heart, lungs and abdomen were negative. The neck was very stiff and painful on motion, and there was tenderness along the entire spine. Kernig's sign was positive and the reflexes were active and equal. There was weakness of the left external rectus muscle with diplopia to the left. The right pupil was larger than the left, but both reacted well to light and accommodation. There was slight weakness of the left side of the face, and hearing was poor in both ears. There was diminished sensation over the entire right side of the body, but vibration and position senses were normal. Motor activity was normal, and there were no signs of cerebellar abnormality.

The temperature was 100.5°F., the pulse 47. The respirations were 26.

The urine examination was negative. The blood showed a red-cell count of 4,900,000 with 80 per cent hemoglobin and a white-cell count of 12,000 with 80 per cent polymorphonuclears. A blood Hinton test was negative. A lumbar puncture showed an initial pressure of 350 mm. with normal pulse and respiratory oscillations. The spinal fluid was pink in color and contained 15,625 crenated red cells and 270 white cells per cubic millimeter; 78 per cent of the latter were polymorphonuclears. The Wassermann test was negative, the goldsol curve was 1333332100, and the sugar was 60 mg. per cent.

X-rays of the skull and spine showed no evidence of fractures.

A second lumbar puncture two days after entry showed an initial pressure of 350 mm. The fluid was xanthochromic and contained 960 red cells. His condition improved slowly, and in two weeks he had only slight residual stiffness of his neck. At that time a lumbar puncture showed an initial pressure of 155 mm. The fluid was clear and colorless and contained no red cells, but did contain 25 lymphocytes. He was discharged on the twenty-first day.

Final admission (six months later). The patient remained perfectly well until the morning of entry when, while cranking an automobile, he suddenly developed severe pain in his head and neck. He went to work but felt sick and somewhat confused and therefore returned home later in the morning. He was given morphine, which afforded relief. Soon afterward, however, he became restless and vomited several times. The pain became more and more severe, and he finally lapsed into a semistupor.

Physical examination revealed a well-developed and nourished man in a semistuporous condition. His head was held back, his eyes were closed, and he was very restless. There was boardlike stiffness of the neck, and the Kernig sign was positive. The right pupil was larger than the left, and they reacted very slightly to light. There was blurring of the left optic disk. The reflexes were equal and active, but there were bilateral Babinski signs. The blood pressure was 110 systolic, 75 diastolic.

The temperature was 100.5°F., the pulse 80. The respirations were 27.

A lumbar puncture showed an initial pressure of 175, and the spinal fluid was grossly bloody. It contained 700,000 red cells and 500 white cells.

After a few hours he lapsed into a deep coma

and began to have Cheyne-Stokes respirations. Two ventricular taps were done, both yielding grossly bloody fluid under a pressure of 360 mm. He died on the day of entry.

Differential Diagnosis

Dr. Henry R. Viets: In summary this is a man of thirty-one who had three injuries to his head. At the age of nineteen he slipped and hit the back of his head, but he made a perfect recovery after a period of headache and vomiting. The second one was when he was twenty-nine, ten years later, and the third at thirty-one. A fourth and final cerebral episode resulted not from traumatic injury but from a strain six months later. It would seem as if we ought to connect all these episodes. The principal thing is that at each time he recovered practically entirely. He did have diplopia after the one at the age of twenty-nine which persisted, but from the first and third he made a complete recovery, which would suggest that we were not dealing with intracerebral disease but with intracranial disease on the surface of the brain. This and the evidence from spinal fluid examinations on the last two entries speak for subarachnoid hemorrhage. We make that diagnosis today more frequently than we ever did before. Blood in the spinal fluid in a young patient who recovers is practically always due to aneurysm. Occasionally we think of tumors, especially the blood tumors such as the angiomas. In spite of the fact that they are often on the surface they seldom bleed but give rise to Jacksonian epilepsy, which this patient did not have. The hemangioblastomas are practically always in the cerebellum and do not give rise to subarachnoid hemorrhage. We think, therefore, of aneurysm giving rise to four episodes of bleeding in this young man without very definite localizing signs. We shall have to say, knowing that aneurysms are usually in the circle of Willis and seldom elsewhere in the cranial vessels, that the aneurysm in this case was probably in the circle of Willis. I am not definitely able to say which part. The evidence for localization is not very good. He had a diplopia the last two years that may have been due to blood's penetrating the sixth nerve, but with its long intracranial course this sign does not help much in localization. He had weakness of the left side of the face. That would make us think of a lesion on the right side. On the other hand he had loss of sensation on the whole right side of the body, which would make us feel certain he had a lesion on the left side. He may have had two lesions, one on each side. It would seem that syphilis was not a factor. He is too young for arteriosclerosis, and it seems as though he had the usual congenital type of aneurysm which continued to bleed from time to time giving this picture of chronic subarachnoid hemorrhage. The last and fatal one bled into the ventricles since the ventricular tap showed blood. He had bilateral Babinski signs and other more serious signs which are consistent with deep bleeding into the ventricle as well as the subarachnoid space.

Dr. Tracy B. Mallory: Dr. Ayer, have you any comment?

Dr. James B. Ayer: This man apparently had had attacks of bleeding nearly half his life. The one on the last entry happened when he was cranking his automobile. In other words something gave way on effort whereas the others were traumatic. I think the duration is enough to rule out most tumors. The hemangioma may run a long course but as Dr. Viets said does not bleed spasmodically in this particular way. One would think of aneurysm or malformation of vessels rather than tumor. One questions whether some disturbance of vessels might occur from trauma which would subsequently bleed more easily. There might be a double lesion. Dr. Kubik has spoken of a good many cases with double or multiple aneurysms.

There is one localizing sign in the first episode. He had double vision, and double vision is common, as Dr. Albright first pointed out to us, in third-nerve palsy. It occurs in 50 per cent of the cases of aneurysm of the middle cerebral artery or at the junction of the cerebral and posterior communicating artery, which is the favorite place.

Dr. Viets: The record says that there was weakness of the left external rectus muscle so it was sixth- and not third-nerve involvement. That is why I tried to point out that it did not help.

Dr. Ayer: This also fits in with Dr. Kubik's analysis of aneurysms to the effect that effort alone is often an explanation of bleeding. Several of our patients have had hemorrhage from the aneurysm on straining at stool.

Dr. Mallory: By all odds the majority of vascular lesions that we find in patients with a history like this are arterial aneurysms in the neighborhood of the circle of Willis, but this case was not. It was a distinctly more unusual condition, which Dr. Kubik will describe.

Clinical Diagnosis

Subarachnoid hemorrhage, recurrent.

Dr. Viets's Diagnoses

Subarachnoid hemorrhage, recurrent.
Aneurysms, circle of Willis?

Anatomic Diagnoses

Hemorrhage, ventricular and subarachnoid.
Aneurysmal varix.

Bronchopneumonia.
Pulmonary congestion and edema.
Hydrohemothorax, bilateral.

Pathological Discussion

Dr. Charles S. Kubik: Out of the cases of spontaneous subarachnoid hemorrhage which have come to postmortem examination in this hospital in the last seven or eight years, ruptured intracranial aneurysms accounted for 18, and I should say that not more than 6 or 7 were due to other causes, venous anomalies and hemangiomas of the choroid plexus being responsible for the majority. Considering the statistics and the similarity of the clinical manifestations produced by subarachnoid hemorrhage resulting from these various causes, ruptured aneurysm would be the logical diagnosis for anybody to make in this case. What we found was a saccular enlargement, 1.5 cm. long and 0.7 cm. in diameter, of a small vein lying against the inner surface of the left optic thalamus and entering the great vein of Galen with the left choroidal vein. Several very small, tortuous veins emptied into the sac. No connection with any of the arteries could be demonstrated.

Dr. Mallory: We do not ordinarily think of varicose veins as being of importance in cerebral lesions, but that seems to be essentially what we were dealing with here.

CASE 24122

Presentation of Case

A forty-three-year-old Scotch laborer entered the hospital with the complaint of headaches of eighteen days' duration.

Eighteen days before entry while at work he noticed a sharp pain in the back of his neck and in the occipital region. He lay down for a while and then went home. The following day he went to see his doctor who prescribed Pluto Water. The next day he drove from Boston to New Brunswick on his vacation. His headache had continued intermittently and on the automobile trip was severe enough to prevent him from doing much of the driving. The headache continued during the subsequent two weeks and occasionally radiated to the frontal region. It was not sufficiently severe to keep him from having a fairly good holiday. Two days before entry his wife heard him make a very irrational statement which she knew to be wholly untrue. At the time of entry the patient was unable to give a clear-cut history. There were no data recorded relative to the mental changes during the two days prior to entry. All the information was given by his wife, who was considered reliable.

His past history, so far as it could be obtained, was almost entirely negative. There had been a loss of 15 lb. during the six months preceding his entry. He had no history of previous cerebral symptoms or of injuries of any importance. He had worn glasses for twenty years and had had them changed three months before entry. The diagnoses at that time were compound hyperopic astigmatism, hyperopia, and presbyopia. There was an indefinite history of a penile sore many years before entry. His wife had had one full-term child, which died twelve days after birth, and three subsequent miscarriages. The family history was otherwise negative.

Physical examination revealed a well-developed and nourished middle-aged man. The heart, lungs and abdomen were negative, and the blood pressure was 140 systolic, 105 diastolic. He was somewhat disoriented and continually grasped the back of his head with his hands and grimaced as if in severe pain. He had no speech difficulty and yet was very slow in answering questions. There was no astereognosis. The Romberg sign was negative, and there was no nystagmus. Complicated movements were poorly performed, but the finger-to-nose and heel-to-knee tests were negative. The pupils were irregular, the right being larger than the left. The left pupil did not react directly to light, but did so consensually. The right reacted normally. The fundi were normal but the visual fields could not be determined. The cranial nerves were otherwise negative. Sensation was intact throughout, and motor activity was normal. The reflexes were active and bilaterally equal.

The temperature was 98.6°F., the pulse 75. The respirations were 18.

The urine examination was negative. The blood showed a red-cell count of 5,030,000 with a hemoglobin of 80, and a white-cell count of 12,500 with 73 per cent polymorphonuclears. The blood Hinton test was negative. A lumbar puncture showed an initial pressure of 210 mm. with normal pulse and respiratory oscillations. The spinal fluid was clear and contained 6 lymphocytes per cubic millimeter, 47 mg. per cent of protein, and 76 mg. per cent of sugar. The goldsol curve was 0000000000, and the spinal fluid Wassermann was negative.

X-rays of the skull showed a calcified pineal gland displaced downward and backward. The pineal was not seen in the anteroposterior view.

His condition remained essentially unchanged for six days except that he became incontinent of urine and definitely drowsy. On the seventh day a ventriculogram was done. Dr. Hampton's report reads as follows: "The lateral ventricles are incompletely filled with air. There is no air in the third and fourth ventricles. The anterior and

inferior horns of the lateral ventricles are well demonstrated. The anterior horns are markedly displaced toward the left but they are approximately normal in size. There appears to be a filling defect in the body of the right lateral ventricle, and the body of the left lateral ventricle is incompletely filled at the same point. The inferior horn on the right is small and displaced downward whereas the inferior horn on the left is dilated and in normal position."

On the same day an operation was performed.

Differential Diagnosis

Dr. Robert S. Schwab: In discussing the differential diagnosis I shall divide the symptoms and points in the history into three groups. First, those which I consider irrelevant, secondly, those which may be relevant, and thirdly, those I feel sure are relevant. The giving of Pluto Water, his wife's miscarriages, and the question of penile sore with negative Hinton and spinal fluid Wassermann I consider irrelevant. Now as to the second group — those that might be relevant — we have eye trouble. I presume he must have been to an oculist to get the eye diagnoses. He had lost 15 lb. in weight. He had a white count of 12,500 with 73 per cent polymorphonuclears. He also had slightly elevated spinal-fluid sugar and protein. As to third group I believe the following are definitely relevant: the left pupil fixed to light but with indirect consensual reflex to light, and the normal right eye; he also made an irrational remark; he could not perform complicated movements; he was stuporous and drowsy; the pineal was displaced downward and backward; the ventricular system was pushed to the left and there appeared to be a filling defect in the right ventricle; he also had pain in the back of the neck and head and incontinence of urine. As to location of the lesion, I do not believe it was frontal because the anterior horns were filled. It was not parietal because the reflexes were normal and there was no motor-system or pyramidal-tract involvement. He had no temporal lobe symptoms, such as astereognosis. We have no evidence of blindness (he did some driving on the way to Nova Scotia) so I presume it was not occipital. We have left, therefore, the region near the midline on the right side, as evidenced by the ventricles' being pushed to the left. It must be somewhat deep, and the regions which come under suspicion at this point are the corpus callosum, third ventricle, or the cortex above the corpus callosum and thalamus on the right.

He had an apparently fixed pupil when tested with direct light, but a good consensual reaction when the other eye was exposed to light. The Argyll-Robertson pupil does not do that. It is fixed to both consensual and direct light. The only lesion that can cause a fixed left pupil with a normal light reflex from the right eye without other involvement of the sixth, fifth and third nerves would be a lesion in the right superior colliculus, that is near the posterior part of the corpus callosum, which is very close to the thalamus. In the differential diagnosis of this expanding lesion I should consider a tumor as most likely at this man's age. His symptoms were rapidly progressive, and a tumor in that region could easily result in such a clinical course. Secondly, I should think of cyst, and thirdly, abscess. Gumma and tuberculoma are fourth and fifth because of normal spinal fluid and negative Hinton and no evidence of tuberculosis elsewhere. To sum up, I should say he had a tumor in the region of the posterior part of the corpus callosum, either in it or above it, extending well to the right side of the midline.

Dr. Aubrey O. Hampton: I cannot go farther than the report in the record. There seems to be a deep mass almost amputating the center of the body of the right lateral ventricle.

Dr. Tracy B. Mallory: The diagnosis that Dr. Schwab has made is approximately the same as that made on the ward.

Dr. James C. White: My diagnosis was right-sided tumor, with the question of whether it involved the frontal or temporal lobe. His mental changes were more noticeable as you talked with him than one would realize from the history here. I believed it was rapidly growing because the symptoms were of such short duration, and the prognosis seemed to be very poor. I thought it was probably spongioblastoma multiforme.

Dr. Mallory: The operative findings were very much of a surprise. Perhaps Dr. White will tell us about them.

Dr. White: As soon as we had the bone flap turned down we could see bluish discoloration of the dura and it was obvious he had a hematoma. On opening the dura the hematoma appeared to cover the entire hemisphere and was a centimeter in thickness. There was a typical neomembrane surrounding the clot, and it was possible to dissect it out over the entire area.

Dr. Mallory: How often do you see a subdural hematoma in a case with no history of trauma?

Dr. White: We have seen several where we could not get a history. One patient I recall had bilateral subdural hematomas. He was an alcoholic and could give no accurate history.

Dr. William B. Breed: How is the patient now?

Dr. White: The patient died. It looked for a while as if he were going to recover consciousness. The afternoon after operation he was mumbling

a little bit and making some movements, but next morning the coma was deeper. In spite of the ventricular shift we thought there might be a good-sized clot on the other side, as frequently happens, so I made a drill hole there but found nothing. The patient died four hours after that. In our experience patients who have had this degree of compression of the brain for a long period often die even though you remove the whole hematoma.

Preoperative Diagnosis

Right frontal brain tumor.

Dr. Schwab's Diagnoses

Brain tumor, right hemisphere over posterior part of corpus callosum?
Cyst in the same region?

Anatomical Diagnosis

Subdural hematoma, right.

Pathological Discussion

Dr. Charles S. Kubik: There was, so far as I can see, no good clue to the diagnosis. Since the specimen from this case reached us in fragmentary form after the surgical removal, let me demonstrate the lesion from another unoperated but essentially similar case. The collection of blood, covering a large part of the lateral surface of the hemisphere, is enclosed between the dura on the outside and a thin, transparent, but fairly strong, fibrous membrane on the inside. The membrane arises entirely from the dura and is nowhere adherent to the underlying arachnoid. The hemorrhage, probably venous in origin, becomes surrounded by a membrane of newly formed connective tissue and, as the blood breaks down, the complex molecules likewise break down, the number of molecules increases and the material takes up fluid by osmosis. The encapsulated hematoma thus continues to increase in size and intracranial pressure rises. This is the brain from the case which was discussed and here are the remnants of the right-sided hematoma. There is flattening, though not very pronounced, of the convolutions of the left hemisphere and some displacement. Here, however, the third ventricle swings distinctly over to the left.

Dr. Schwab: How do you explain the pupillary findings?

Dr. Kubik: I have no explanation for them.

A Physician: Was there any evidence of vascular disease?

Dr. Kubik: No.

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AN OPPORTUNITY FOR THE DISTRICT MEDICAL SOCIETY

The Medical Society of the County of Westchester, New York, has adopted a periodic medical examination for adults in contact with children. This examination, which is performed at a special rate, includes particularly physical examination, a chest x-ray and a Wassermann test. After each semiannual examination, a medical card is issued to those who have no serious physical handicaps and have been found free from evidence of communicable disease.

Teachers, nurses and domestic servants naturally constitute the group toward which the efforts of the medical society are directed, and parents are urged to co-operate by insisting that these individuals who are in contact with their children hold medical health cards. In this way a class of "health certified servants" may be created whose services will be more desirable and hence will draw better wages. Both employer and employee will benefit by such a co-operative scheme, far more desirable than any attempt at instituting compulsory examinations.

Legislation at best can go only a short distance in prescribing personal health measures; case finding in communicable disease has always been accomplished by the practicing physician or by voluntary co-operation on the part of the patient. Ill-health and uncleanly habits in servants are unmeasured but very potent sources of danger. The organization of health services patterned after that of the Medical Society of the County of Westchester might logically be recommended to our various district societies.

A YEAR OF HEALTH

The health of the citizens of Massachusetts during 1937, according to the report of Commissioner Henry D. Chadwick, was distinctly above par. It will go on the record as a "healthy" year, with no epidemic of any dangerous communicable disease, and a decrease in the morbidity of most of the other reportable illnesses.

Of forty communicable diseases, about 98,000 cases occurred in 1937 as against 106,115 in 1936, a decrease of nearly 8 per cent. Diseases which, within a few years, were dread names to conjure with, are now of little moment. Typhoid fever, for instance, which ran as high as 3452 cases in 1910, occurred in barely over 100 cases in 1937. Diphtheria, with 10,322 recorded cases in 1917, showed less than 300 in 1937, and smallpox has not occurred within the State since 1932. The death rate from tuberculosis has halved within a generation, 1937 producing only about 5200 cases with 1730 deaths.

The virulence of the streptococcus of scarlet fever has decreased so markedly in recent years that it is now necessary to go to Russia or Roumania to study the disease in its old form, and in general a similar experience seems to have been encountered

with other forms of infection caused by hemolytic streptococci.

Health runs in cycles with recurrent epidemic years of the various infectious diseases, but over a long period of time many of the infections have decreased in severity and methods of immunization have been developed for others of them. The expectancy of life has steadily lengthened as the infectious diseases have lost in virulence or have come under control, and more and more prominently the degenerative diseases of middle and later years stand out as our principal causes of death.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

M. Fletcher Eades, M.D., *Secretary*
19 Bay State Road
Boston

Case History No. 64. Premature Separation of the Placenta

Mrs. L. D., a seventeen-year-old primipara, was admitted to the hospital in convulsions when she was approximately thirty-eight weeks pregnant. Three weeks before entry she consulted a doctor for the first time, and he had examined the urine and pronounced it negative. There was some edema of the ankles at that time but no other signs or symptoms of toxemia. Edema of the face developed during the week preceding entry. The patient went to bed at 10 p. m., May 26, apparently in good health. She awoke at 1 a. m. complaining of pains in the abdomen and she vomited. At 3 a. m. there was a generalized convulsion lasting several minutes. The patient had four more convulsions before entry to the hospital at 5 a. m. and she never regained consciousness. During the seizures she voided involuntarily and frothed at the mouth.

The family history was negative for tuberculosis, cancer or nervous disease. Her mother died of blood poisoning following a miscarriage. Her father was living and well.

The patient had always been well. She had measles in childhood. There was no history of scarlet fever, septic sore throat, rheumatic fever, diphtheria or typhoid. The systems were negative. Her menstrual history was not elicited.

A series of selected case histories by members of the section will be published weekly.
Comments and questions by subscribers are solicited and will be discussed by members of the section.

Physical examination revealed a well-developed, slightly obese young woman in coma and with stertorous breathing. The face was edematous, particularly about the eyes. The skin was dusky. The eyes were normal except for dilated pupils. The heart was not enlarged, the rate was regular, the sounds were of good quality, and there were no murmurs. Blood pressure was 228 systolic, 130 diastolic. The chest was symmetrical, expansion was equal and normal, and the lungs were clear. The abdomen was enlarged to the size of an eight and one-half months' pregnancy. Labor pains were noted about every five to seven minutes. The fetal heart was not audible. There was marked edema of the feet and ankles.

Soon after entry the patient was given gas-oxygen anesthesia and was catheterized. The urine boiled solid with albumin and there were many hyaline and granular casts. She was given morphine gr. ¼ subcutaneously, and 20 cc. of 10 per cent magnesium sulfate intravenously. She had one convulsion fifteen minutes after entry and another ten minutes later. Slight twitching of the face was noted three hours after admission. She was then given 15 cc. of magnesium sulfate intravenously and 360 cc. of blood was removed by venesection. The systolic blood pressure fell to 170. The pulse was 72. At 9 a. m., four hours after entry, vaginal bleeding appeared, the uterus became spastic and there were no intervals of relaxation. The pulse rose to 140 within thirty minutes. A diagnosis of premature separation of a normally implanted placenta was made and immediate preparation was undertaken for delivery by cesarian section.

Under gas-oxygen anesthesia a low classical cesarian was performed without difficulty. The baby was stillborn. The placenta was separated over approximately one-half of its surface, and there was a moderately large retroplacental clot. There was no free blood in the uterine cavity. The uterine musculature was not abnormal in either appearance or texture. Bleeding was not excessive and was controlled by the intramuscular injection of 0.5 cc. of posterior pituitary extract. The patient's pulse was very weak at the conclusion of the delivery but improved markedly following a transfusion of 600 cc. of citrated blood.

The pulse dropped to 90 following delivery and the patient's general condition seemed improved. Suddenly she developed Cheyne-Stokes respiration and irregularity of the pupils. There was a short convulsion at 2:40 p. m., and she died at 2:48 p. m. At no time following the operation had vaginal bleeding been excessive and there had been no signs suggestive of internal hemorrhage. It was felt that death could largely be attributed to eclampsia, and that the premature separation of the normally implanted placenta was an incidental occurrence

which added to the shock and jeopardized the patient's chances for recovery but was not actually the cause of death.

Postmortem examination showed enlargement of the liver to 2220 gm. The organ was smooth and irregularly mottled with dark-red and light-yellow spots. The kidneys were grossly normal, as were the uterus and the brain. Microscopic examination revealed small subendocardial hemorrhages of the heart; numerous extensive periportal and interlobular hemorrhages of the liver with resulting degeneration and absence of liver cells; and swelling of the glomerular tufts of the kidney. The adrenal, cerebrum, cerebellum, pituitary and uterus were all normal. The findings were those of eclampsia.

Comment. The prognosis was very unfavorable when this patient entered the hospital. The subsequent separation of the placenta made the prognosis even graver. The prenatal care of course was most inadequate. Her one visit to a physician three weeks before delivery showed nothing abnormal except edema. Had she been seen routinely, this edema might well have shown that the patient had put on a great deal too much weight and might have made one suspicious of an impending toxemia. It is perfectly possible that there were no other symptoms at this visit except the edema. Eclampsia occasionally may be as fulminating as in this case. The separation of the placenta, in this instance definitely due to the toxemia, added the element of hemorrhage to the serious eclampsia. The more conservative method now in vogue of rupturing the membranes, packing the cervix, and applying a Spanish windlass certainly would not have added the degree of shock which the abdominal section undoubtedly did, but it probably would have made no difference in the ultimate outcome.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau, have been arranged for the week beginning March 28:

BARNSTABLE

Sunday, April 3, at 4:00 p. m., at the Cape Cod Hospital, Hyannis. Subject: Some Complications of Labor: Analgesics in Labor. Instructor: Christopher J. Duncan. John I. B. Vail, *Chairman.*

BERKSHIRE

Thursday, March 31, at 4:30 p. m., at the House of Mercy Hospital, Pittsfield. Subject: Recent Advances in the Diagnosis and Treatment of Heart Disease. Instructor: Oliver H. Stansfield. Melvin H. Walker, Jr., *Chairman.*

BRISTOL SOUTH (Fall River Section)

Monday, March 28, at 4:30 p. m., at the Union Hospital, Fall River. Subject: Bleeding in the Last Trimester of Pregnancy. Instructor: Meinolf V. Kappius. Howard P. Sawyer and Robert H. Goodwin, *Chairmen.*

ESSEX NORTH

Friday, April 1, at 4:30 p. m., at the Lawrence General Hospital, Lawrence. Subject: Bleeding in the Last Trimester of Pregnancy. Instructor: Judson A. Smith. John Parr, *Chairman.*

FRANKLIN

Wednesday, March 30, at 8:00 p. m., at the Franklin County Hospital, Greenfield. Subject: Rheumatic Infection; Rheumatic Heart Disease. Instructor: Edward F. Bland. Halbert G. Stetson, *Chairman.*

HAMPDEN

Thursday, March 31, at 4:00 p. m., at the Academy of Medicine, Professional Building, 20 Maple Street, Springfield, and at 8:00 p. m., in the Outpatient Department of the Skinner Clinic, Holyoke Hospital, Holyoke. Subject: Gonorrhea in the Male. Instructor: J. Dellinger Barney. George D. Henderson and George L. Schadt, *Chairmen.*

HAMPSHIRE

Wednesday, March 30, at 4:15 p. m., in the Nurses' Home, Cooley Dickinson Hospital, Northampton. Subject: The Use and Misuse of Prontylin. Instructor: Benjamin W. Carey, Jr. Warren P. Cordes, *Chairman.*

MIDDLESEX SOUTH

Wednesday, March 30, at 4:00 p. m., at the Cambridge Municipal Hospital, Cambridge Street, Cambridge. Subject: Treatment of Burns. Instructor: Patrick J. Mahoney. Edmund H. Robbins, *Chairman.*

NORFOLK

Friday, April 1, at 8:30 p. m., at the Norwood Hospital, Norwood. Subject: Drug Therapy in Pediatrics. Instructor: Warren R. Sisson. Hugo B. C. Riemer, *Chairman.*

Essex North District Medical Society

Attention of the members of the Essex North District Medical Society is called to the fact that the hour of assembly for postgraduate courses of the Massachusetts Medical Society being held in Lawrence this spring has been changed to 4:30 p. m.

John Parr, M.D., *Chairman.*

DEATHS

ADAMS — Donald Stansbury Adams, M.D., of 27 Westwood Drive, Worcester, died March 13. He was in his sixty-sixth year.

Born in Indianapolis, Indiana, he attended the schools in that city. He received his degree from the University of Virginia Department of Medicine in 1917 and interned at the University Hospital and the Boston City Hospital. During the war he served in the Medical Corps of the U. S. Army at Fort Devens. While there he met Dr. Homer Gage who persuaded him to go to Worcester, where he became resident surgeon at the Memorial Hos-

pital. He began private practice in 1923, but remained on the staff of the Memorial Hospital as assistant surgeon. He was, in addition, consulting surgeon at the Masonic Hospital, Shrewsbury, the Harrington Memorial Hospital, Southbridge, and the Webster District Hospital.

Dr. Adams was a fellow of the American Medical Association and the Massachusetts Medical Society. Among his affiliations were memberships in the American College of Surgeons and the New England Surgical Society. He was a major in the Medical Reserve Corps.

His mother survives him.

CRANDELL — Arthur Richmond Crandell, M.D., died at his home, 48 Church Green, Taunton, March 19. He was in his sixty-ninth year.

A native of Taunton he attended the high school there, later graduated from Harvard University and received his degree from Harvard Medical School in 1896. Dr. Crandell was a fellow of the American Medical Association and the Massachusetts Medical Society. His memberships included the New England Pediatric Society, the Taunton Doctors' Club, the Harvard Clubs of Boston and Taunton, and the Old Colony Historical Society. Since 1900 he had been consulting physician at the Morton Hospital in Taunton.

His widow, a daughter, a sister and three grandchildren survive him.

NEW HAMPSHIRE MEDICAL SOCIETY

HISTORICAL NOTES

The New Hampshire Medical Society was incorporated by a legislative act signed on February 16, 1791. Dr. Josiah Bartlett, president of the Senate, was one of the nineteen charter members who met at Exeter the following May for formal organization. Dr. Bartlett, senior member of a family which has furnished five active officers and fellows to the society, was later president, and while governor of the State, refused a re-election. In his letter declining further honors he expressed the hope that the new society would "produce effects greatly beneficial to the community, by encouraging genius and learning in the medical science and discouraging ignorant and bold pretenders from practicing an art of which they had no knowledge." He set forth the aims of the society in the promotion "of better regulations than it had," and expressed the wish that "the practice of medicine in the State (upon which the lives and healths of our fellow citizens depend) might be under better regulation than in times past." John Rogers, of Plymouth, attended this meeting coming on horseback, a journey more laborious and time-consuming than would be necessary for a trip to the West Coast today.

David Ramsay, early pioneer physician, wrote one of the first and best histories of the Revolutionary War. It is still accepted as a classic.

The preceptor system prevailed in the State for many years. Medical schools then required that each attendant on a course of lectures be registered with a practitioner. It is reported that one popular physician in Portsmouth had twenty students at a time. When Dr. Willard Parker left New Hampshire on his lecture tour from school to school, as he did for a considerable period each year, pupils followed him. Dr. Frank Foster, of New York, in a short sketch of the career of Dr. Charles Gage, of Concord, a leading surgeon for many years, states that Dr. Gage always had many students, and that he himself studied with him for five years before venturing to attend a medical school.

It is interesting to note the frequency with which men, even in the very early days of New Hampshire, traveled and studied in foreign medical schools, both before and after graduation. Records show many instances of tremendous sacrifice involved in an absence from practice of many months, resembling the career of John Y. Bassett, of Huntsville, Alabama, "The Alabama Student," immortalized by Osler in one of his finest essays.

Two New Hampshire members of the Continental Congress were Drs. Matthew Thornton and Josiah Barlettt, both signers of the Declaration of Independence. Bartlett was the first member to vote in favor of it, and at the signing of the document his name appears immediately after John Hancock, the president. "He had many times taken the responsibility for the birth of a man. Why should be shrink at the birth of a nation?" Dr. Thornton and Dr. Bartlett, like Benjamin Rush, of Pennsylvania, were young men, who showed the fiber of which they were made in their subsequent careers in medicine and in public service.

In its first century the New Hampshire Medical Society received seven hundred and twenty-four men into membership. The membership numbered two hundred and forty-five at the centennial exercises in 1891, and it was reported that honorary membership had been conferred on seventy physicians.

Conservative New Hampshire was slow in admitting women physicians to membership. By her association with the Manchester Medical Association, Dr. Mary Danforth became a member of the Society in 1877. Dr. Julia Wallace-Russell, of Concord, in June, 1878, was voted the first woman member through action of the Council.

Following the vote of the Society in 1838 regarding the desirability of a national convention, the Medical Society of the State of New York recommended that the first meeting be held at Philadelphia in May, 1840. In 1839, "at Smith's Tavern in Salisbury," Luke Howe, Thomas P. Hill and Thomas Chadbourne were chosen as delegates to the Philadelphia convention.

Dr. William E. Maloney, of Keene, showed before the Cheshire County Medical Society in 1894 a patient on whom he had performed a cholecystectomy a few weeks before. This is undoubtedly the first removal of the gall bladder ever done in the State.

Adhesive-plaster traction in the treatment of fracture of the femur originated with Josiah Crosby, of Manchester, who was of the family that gave many eminent medical men to this State. In 1849 an engineer, building a bridge over the Merrimack for the New Hampshire Central Railroad, suffered a fracture of the upper third of the bone. Dr. Crosby applied, as was then customary, a long splint with a gaiter for extension and perineal band for counterextension. The patient bitterly complained of the pull of the gaiter about the ankle and instep. At his first removal from the bed the fragments parted, and the patient was informed that the apparatus must again be applied. Rebellion followed, and the doctor was urged to consider some less painful method of treatment. Long straps of adhesive plaster were applied to the sides of the leg, contact assured by snug bandages, and a weight attached. The fracture united and the patient lived many years. To distinguish Dr. Crosby from a nephew of the same name he was ever after known as "Sticking-Plaster Crosby." A writer in the *Philadelphia Medical Examiner* in 1852 attempted to claim priority for the discovery, but the writer's contentions were never accepted.

The income of physicians of the past is always of inter-

est to us moderns. A leading physician of our most wealthy city is reputed to have received no more than five thousand dollars per year in his most productive period, the late 1870s. He was paid seventy-five dollars for his largest day's work. On the basis of seventy-five cents per visit, a dollar and half for night visits, and a five-dollar obstetrical fee, one had to be industrious. A receipted bill of 1829 recently came to light with charges of "twenty cents for calling in and emetic" and "two dollars fifty cents for facilitating the birth of a child." Yet not a few were able to leave modest competencies for their families.

At the meeting of the Society in 1894, Cyrus Kelley, in a paper "Then and Now," stated that the only instrument of diagnosis he owned in the early days of practice, aside from a crude clinical thermometer, was a stethoscope of cardboard, rolled into the shape of a cone, the base being applied to the chest and the apex to the ear. Laennec had just reported his observations on transmission of sound from the chest, but the wooden stethoscope had not then been offered. Even percussion came later.

Agitation for state licensure began as early as 1890, but the efforts of the organized profession were nullified by sectarian groups and reluctant legislators. The year 1897 marked the enactment of the first comprehensive statute for adequate protection of the public, and this statute has required very little amendment to the present. From July, 1897, when the law became operative, to 1938 over twenty-one hundred licenses have been granted. An average of about five hundred physicians have been in active practice each year.

At the 1895 session of the Society, following a discussion of the treatment of diphtheria, Dr. O. B. Douglas, of New York City, a prominent laryngologist, is quoted as saying: "I do not believe that anti-toxine has come to stay. Professor Winters recently gave us [at the New York Academy of Medicine] an *exposé* of its use at Willard Parker Hospital. It seemed to do more harm than good."

Probably no other New Hampshire physician had, or ever can have, the unique distinction of Nathan Smith. A pupil of a prominent Vermont surgeon for a short time, he started a practice at Cornish, but two years later, realizing his incompetence, he registered at Harvard and received the degree of M.B. in 1790. He studied abroad returning six years later when he was honored by the degree of A.M. by Dartmouth College, and was elected to the Chair of Anatomy, Surgery, Chemistry, Materia Medica, and Theory and Practice in the medical school he was opening. In one room in Dartmouth Hall — laboratory, lecture room, library and dissecting room — he taught for four years. In 1811 Yale called him to New Haven to inaugurate the medical department. In 1821 he organized the medical school at Bowdoin College, giving all the lectures for two years, except those on chemistry and anatomy. Though he continued his lectures at Yale from 1813, he managed to hold a professorship in surgery and medicine at the University of Vermont. "To him more than to any other man, it is believed, may be ascribed the advantages for medical education in America at this date [1891]."

CANCER COMMITTEE

Biopsies

The most accurate method for the diagnosis of cancer is the microscopic examination of a portion of the tumor in the hands of an expert pathologist.

Details for performing biopsies vary with the individual situation; some are performed with the scalpel, others with the electric knife, some by one or other of several punches which are on the market, and some by curettage. *In any case a living and not a necrotic part must be removed, preferably with a bit of the surrounding tissue.* Merely clipping off of the surface of a tumor is not adequate.

The best fixative is 10 per cent formalin solution. The tissue should be immediately placed in a volume about ten times as great as the mass of tissue removed.

Biopsy is of value in following the course of treatment, — sometimes of critical value, — and *if properly done, it is harmless.* Details of the history are of importance to the pathologist in all cases and should always be sent with the specimen. This is particularly important in those in which physiological activities are likely to be superimposed in and around tumors, such as menstrual hyperplasias in carcinoma of the uterus.

Occasionally a clinical diagnosis of cancer is not sustained by the microscopical picture, whereupon a *consultation with the pathologist is imperative.*

Biopsies are harmless if done properly; they usually settle the diagnosis; but pieces of tissues must be properly chosen for this purpose. They are also necessary in many cases to follow the course of treatment. The pathologist can be depended upon to use methods of preparation of his materials to ensure the quickest reports consistent with the accuracy demanded.

There is more danger from massage or repeated manipulation in making examinations, especially in cancer of the breast, than in doing a biopsy.

Howard N. Kingsford, M.D.,
Committee on Control of Cancer.

PNEUMONIA SERVICE

Dr. Travis Burroughs, secretary of the New Hampshire Board of Health, has issued detailed information regarding the pneumonia service. Complete instructions for typing sputum and for obtaining serum will be furnished on application. Arrangements have been made for designation of hospitals and laboratories for typing in various parts of the State, and, as rapidly as possible, more technicians will be trained for this work. The plans of the secretary include as complete a service as is offered by any other state. Only technicians with proper training and a high standard of performance will be offered the special course, so that a uniform and efficient service will be obtained, without waste of effort and money.

COMMONWEALTH FUND FELLOWSHIPS

Announcement is made by the Committee on Medical Education and Hospitals that Commonwealth Fund fellowships are available, for members of the Society, in medicine, pediatrics, obstetrics and office surgery. Fellows must be graduates of Class "A" medical schools, residents of communities of less than ten thousand population and must have been in practice at least five years. A generous stipend is allowed for expenses, and tuition is paid by the Fund. Application blanks may be obtained from P. O. Box 48, Hanover, N. H. Dr. Samuel T. Ladd, president of the Society, has endorsed this plan, and urges eligible physicians to make application.

SOCIETY NEWS

Dr. Sven Gundersen, of Hanover, read a paper on "Serum Treatment of Pneumonia" at a meeting of the Carroll County Medical Society at Conway on February 20.

Dr. Edna Walck, the first woman member to be honored with the presidency of the Dover Medical Society,

was in the chair for the regular meeting on March 2, when Dr. George Cumming, of Portland, gave a clinical talk on "Nose and Sinuses." This society is one of the oldest city associations in the country with continuous existence, having been organized in 1849.

Frank Sulloway, Esq., legal adviser of the Society, was the speaker at the February meeting of the Dover Medical Society. His subject was "Medical Liability."

BIRTH

On February 27, to Dr. and Mrs. Samuel J. King, of Farmington, a son, Robert Bruce.

PERSONALS

Dr. Roscoe Blanchard, of Dover, has recovered from a recent illness and has resumed his practice.

Dr. Peter F. Doyle has been elected city physician of Dover for the term 1938-39.

Dr. Nathan Milliken, of Hanover, has been elected an associate of the American College of Physicians.

Dr. Ralph Miller, of Dartmouth Medical School, was a delegate to the recent meeting of the Council on Medical Education and Hospitals at Chicago.

Dr. Montfort Haslam, formerly resident physician at St. Paul's School, Concord, opened an office at 18 Church Street, Littleton, on March 1. Dr. Haslam has been for the past year in New York City, where he has taken postgraduate work at the Post-Graduate Hospital, Willard Parker Hospital and Margaret Hague Maternity Hospital.

Dr. George S. Foster, Manchester, is the donor of the Mt. Washington Marathon Trophy now on display at the New Hampshire Historical Society. The large silver cup already bears the names of two winners who have made the ascent of the mountain in less than one hour and twenty minutes.

NOTES

Representative Charles P. Tobey has introduced a bill in the House of Representatives carrying an appropriation for the establishment of a veterans' administration general hospital in the southern part of New Hampshire.

Announcement has been made by the Manchester Council of Social Agencies concerning the recent formation in that city of a permanent social hygiene committee, with Dr. Harry W. N. Bennett as chairman. This committee is to be expanded to include both professional and lay people and will confine its activities mostly to maintaining a speakers' bureau and literature in the field of social hygiene.

Dr. Ralph Jones gave an address on "The Influence of Medicine on History" for the Whitefield Rotary Club on February 19.

The trustees of the Wentworth Hospital, Dover, announce the appointment of Miss M. A. Hall as superintendent, and the reorganization of the nursing and administrative staff.

Dr. Robert B. Kerr, executive secretary of the New Hampshire Tuberculosis Association, announced in his annual report that there are 6223 active, arrested and contact cases of pulmonary tuberculosis in the State. New Hampshire with a death rate of 33.7 per 100,000 has the lowest rate in New England, and is eighth lowest in the continental United States. Since the association was organized, deaths per year have decreased from 500 to 172.

Dr. Warren Phillips, of Boston, was the speaker at a meeting of the Wolfeboro Rotary Club on February 15. His subject was "What the Layman Should Know of Syphilis." The Tufts College Medical School talking film "The Training of the Doctor" was shown.

Under the direction of Mrs. Harry W. Smith, of Durham, the annual drive for enrollment in the Women's Field Army will be held during the month of April. The State has been divided into districts roughly corresponding to the location of the clinics of the State Cancer Commission. Physician and nurse speakers will address groups of both men and women.

The income of a trust, created by the will of Volna K. Kelton, of Grafton Center, is used for the payment of a bonus to the local physician. Dr. Walter D. Berry has been retained to provide medical service for a group of towns among which are Grafton, Danbury, Orange, and Springfield.

DEATHS

LEETE — George E. Leete, M.D., who had practiced medicine in Concord for the past forty-four years, died at his home, Tuesday, February 22. He was in his eighty-seventh year.

Dr. Leete was born in Claremont, New Hampshire, March 29, 1851, the son of George H. and Sarah F. (Chase) Leete; his ancestors were among the first to settle in Connecticut and later moved to New Hampshire.

He graduated from the Dartmouth Medical School in 1878, after which he established a practice in Canaan where he remained for seventeen years.

In Canaan, Dr. Leete was a member of the School Board in 1893 and of the Board of Health in 1894. The remainder of his life was spent in Concord. The New Hampshire Medical Society gave him its gold medal for fifty years of medical practice in 1934.

On February 14, 1878, he married Katherine S. Sawyer, now deceased. One son, Dr. Edward Don Leete, of Boston, survives him. A second son, George Paul Leete, died.

Dr. Leete was a member of the New Hampshire Medical Society and the American Medical Association. He was also an honorary member of the Jefferson College Alumni Association at Philadelphia.

LOBDELL — Alban J. Lobdell, M.D., died March 5 in Keene after a short illness. Dr. Lobdell had been one of Winchester's most prominent residents since opening his office in 1893. He was interested in community affairs and had served as president of the Board of Trustees of the Winchester Library and as a member of the Board of Health for several years.

Dr. Lobdell was born in East Berne, New York, April 2, 1868, a son of Adoniran J. and Eleanor (Veeder) Lobdell. He started teaching school when eighteen years old and at the same time was studying medicine. He graduated from the New York Homeopathic Medical College in 1893.

He was a member of the New Hampshire Medical Society, the Cheshire County Medical Society and the American Institute of Homeopathy.

On November 25, 1896, he married Miss M. Grace Ball, of Winchester, who survives him. He is also survived by two sons, Alban J. Lobdell, Jr., of Woburn, Massachusetts, and Winston B. Lobdell of Stoneham, Massachusetts; a brother, Rev. Isaac Lobdell, pastor of the Universalist Church in Attleboro, Massachusetts; and two grandchildren.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR FEBRUARY, 1938

DISEASES	FEBRUARY 1938	FEBRUARY 1937	FIVE-YEAR AVERAGE*
Anterior poliomyelitis	0	0	1
Chickenpox	1608	1438	1225
Diphtheria	11	17	41
Dog bite	525	572	451
German measles	80	77	503
Gonorrhea	445	429	406
Lobar pneumonia	519	964	651
Measles	811	3502	3539
Meningococcus meningitis	9	15	9
Mumps	777	735	889
Paratyphoid B	1	2	0
Scarlet fever	1213	1002	1058
Syphilis	461	509	401
Tuberculosis, pulmonary	195	252	235
Tuberculosis, other forms	23	21	30
Typhoid fever	5	3	5
Undulant fever	3	1	2
Whooping cough	454	1831	993

*Based on figures for preceding five years.

RARE DISEASES

Diphtheria was reported from: Boston, 2; Fall River, 2; New Bedford, 1; Swampscott, 1; Taunton, 5; total, 11.

Dysentery, bacillary, was reported from: Boston, 2; Brookline, 1; Greenfield, 1; Peabody, 1; Worcester, 1; total, 6.

Meningococcus meningitis was reported from: Boston, 2; Cambridge, 1; Chicopee, 1; Holyoke, 1; Tewksbury, 1; Waltham, 1; Westfield, 1; Worcester, 1; total, 9.

Paratyphoid B was reported from: Belmont, 1.

Pfeiffer bacillus meningitis was reported from: Attleboro, 1.

Septic sore throat was reported from: Beverly, 2; Boston, 5; Brookline, 1; Cambridge, 1; Chicopee, 1; Lawrence, 1; Medford, 1; Melrose, 1; Northfield, 5; Quincy, 1; Springfield, 1; Winthrop, 1; total, 21.

Trichinosis was reported from: Boston, 3; Springfield, 1; total, 4.

Typhoid fever was reported from: Boston, 1; Chelmsford, 1; Haverhill, 1; Quincy, 1; Westfield, 1; total, 5.

Undulant fever was reported from: Chicopee, 1; Natick, 1; Pittsfield, 1; total, 3.

The incidence of diphtheria showed record low figures for the second consecutive month.

German measles, mumps and tuberculosis (other forms) were reported below the five-year average.

Chickenpox for the second consecutive month showed record high incidence.

The incidences of scarlet fever and undulant fever were above the five-year average.

The incidences of meningococcic meningitis and typhoid fever were not remarkable.

Lobar pneumonia, whooping cough, measles and pulmonary tuberculosis were reported at figures considerably below the five-year average.

The reported cases of animal rabies gave evidence of wide distribution throughout the State. New foci were reported in Boxford, Chelsea and Sutton. Previously noted foci in the North Metropolitan area and in Wilmington were active.

TUBERCULOSIS ABSTRACTS

The Effect of Contagious Diseases on Tuberculosis

An attack of acute contagious disease in a child infected with the tubercle bacillus is something nearly every physician dreads. It has long been taught that measles, whooping cough and influenza predispose to tuberculosis and aggravate existing clinical tuberculosis. It is also commonly said that the acute contagious diseases, particularly measles, depress or obliterate the child's capacity to react to tuberculin. These opinions, seldom supported by convincing facts, have recently been challenged. J. P. Nalbant in a paper entitled "The Effect of Contagious Diseases on Pulmonary Tuberculosis and on the Tuberculin Reaction in Children" (*Am. Rev. Tuberc. 36:* 773-777, 1937), reports on a study made of 118 children convalescing from tuberculosis who developed acute contagious diseases while in the sanatorium. Excerpts from his paper follow:

Several writers state that during an attack of measles the tuberculin test becomes negative. Some assert that intercurrent infections, particularly measles, stimulate activity in many cases of tuberculosis. In one series of 37 cases of tuberculous children who developed measles, the tuberculin test done by the Pirquet method showed that the reaction became negative in all at the appearance of the eruption, but became positive again in half of them by the seventh day. Other writers express different views. Chadwick, for example, found that a group of tuberculous children who reacted positively to tuberculin showed no change roentgenologically and no change in their tuberculin reactions during and after measles. Berghoff studied 596 cases of measles in the army and found only 1 case of frank active tuberculosis following directly after a measles infection.

Scattered studies made in Europe to determine the effect of whooping cough, chickenpox, scarlet fever and measles on the tuberculin reaction, and on active or inactive tuberculous lesions, indicate that the effect of the contagious diseases on tuberculosis has been exaggerated and may be very doubtful. This supports the findings of the author in a study made at the William H. Maybury Sanatorium, which included 43 children with measles, 39 with chickenpox, 16 with whooping cough, 13 with scarlet fever, 30 with mumps and 6 with diphtheria, making a total of 147 cases of acute infectious disease in a group of 118 children convalescing from pulmonary tuberculosis of the childhood type. The ages of the children ranged from six months to fifteen years. All had x-ray examinations of the chest a short time before the onset of the contagious disease and directly after the expiration of the quarantine period. Eighty-three of the 118 children had active pulmonary tuberculosis of the childhood type; the remaining 35 had quiescent or apparently arrested disease.

In 4 of the 43 cases of measles the intracutaneous tuberculin test with old tuberculin became negative to a dose to which they were positive before, but was again positive two weeks after the disappearance of the eruption. Six cases showed, by roentgenological examination, an increase in the pre-existing tuberculous process but none of these occurred in less than one month after the measles. In each instance the exacerbation of the tuberculosis was an evanescent occurrence and all recovered completely in a few months.

Two of the 16 children with whooping cough showed exacerbation of the tuberculous disease. In 1 case this occurred during the course of whooping cough but subsided promptly. Three of the cases of chickenpox experienced extensions of their tuberculous lesions: none of them showed any change in the tuberculin reaction. Of the 25 children with mumps, 24 were positive to tuberculin before and after the disease. However, a change in the type of the reaction was noticed in several. None of the

mumps patients showed reactivation or exacerbation of their tuberculosis.

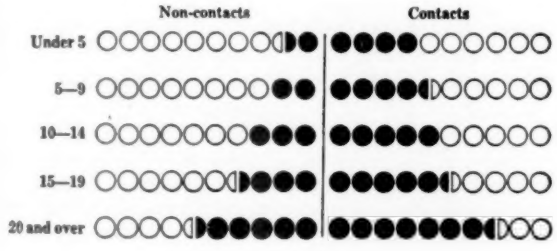
Of the 13 cases with scarlet fever, only 1 showed a spread of the tuberculous process. None of the 6 cases of diphtheria experienced any ill effects so far as their tuberculosis was concerned. The children with scarlet fever and diphtheria were not tested with tuberculin.

In the discussion, the author points out that only 12 children of the 118 showed any increase in the tuberculous lesions during convalescence. This closely parallels the experience of similar groups of patients whose tuberculosis was not complicated by acute contagious diseases. In the great majority of those who showed increase in tuberculosis, the extension occurred several weeks after the intercurrent disease had subsided. None of these remissions occurred in quiescent or apparently arrested lesions showing that the old foci were not disturbed by the intercurrent contagious disease. The remissions seen in the active tuberculous lesions could be safely considered coincidental and unrelated to the contagious disease.

Very little evidence was found to support the contention that measles or any of the other contagious infections have a depressing effect on the body's capacity to react to tuberculin. In the majority of previous studies the Pirquet method was employed for giving the tuberculin test. This may explain the apparent discrepancy, because the Mantoux test, which is more precise, was used in all of the author's cases.

RESULTS OF TUBERCULIN TESTS

Tuberculin reaction studies made with purified protein derivative in various parts of the country were collated by the Statistical Service of the National Tuberculosis Association. The graph, based on 56,688 tests, pictures the



Each circle = 10% of group tested
Solid black = positive Outline = negative

steady increase in the percentage of reactors with increasing age. It contrasts also the far greater percentage of reactors among contacts as compared with those among non-contacts. — *Tuberculosis Abstracts.* March, 1938.

CORRESPONDENCE

FELLOWSHIP IN DIABETIC LABORATORY WORK

To the Editor: A fellowship in diabetic laboratory work for technicians working in other hospitals or in doctors' offices has been created at the New England Deaconess Hospital for the remainder of this year or perhaps longer if it meets a need. Often a graduate technician may require simply a few days' instruction, rarely over one or two weeks.

It has been reported to me that our visiting doctors are often interested particularly in rapid methods for quantitating sugar in the urine, in capillary blood-sugar tests for children and in various measures by which costs are reduced.

The technician will be expected to secure rooming accommodations, but meals will be provided by the hospital and there will be no charge for instruction.

Should a technician care to apply for this fellowship, the application should be accompanied by a letter, addressed to me, from the superintendent of the hospital or doctor by whom he or she is employed.

WARREN F. COOK, *Superintendent.*

New England Deaconess Hospital,
Deaconess Road,
Boston, Massachusetts.

INTERCITY HEALTH-CONSERVATION CONTEST

To the Editor: To the medical profession of Boston, the Boston Health Department expresses its gratitude for the co-operation received from the doctors who gave so generously of their time to compile and place at the disposal of the department data upon immunizations and other public-health measures performed by them for their private patients during the year 1937.

This material was used in the recently completed Intercity Health-Conservation Contest. These contests, sponsored by the United States Chamber of Commerce and the American Public Health Association, have been going on for a number of years. This is, however, the first time that Boston has entered the contest, and the decision to do so was arrived at upon rather short notice and late in the day. Hence, the sudden call upon individual doctors and organized agencies for the necessary data.

The response from private physicians to our request was most gratifying, both as to the number of doctors taking the trouble to answer the appeal and also the volume of what may be classified as public-health or preventive functions, privately performed. For instance, 3328 Boston children were immunized against diphtheria, 6390 children were vaccinated against smallpox, 3000 infants and 1800 preschool children were periodically examined for the purpose of keeping the children well and over 19,000 prenatal visits were made in the private practices of about 25 per cent of the members of the Massachusetts Medical Society with offices in Boston.

This department also thanks all official and voluntary agencies engaged in public-health work which contributed information upon numbers and kinds of public-health functions performed by these agencies during the year 1937, as well as the Committee of Citizens acting for the local Chamber of Commerce, whose members aided in the fact findings necessary for the required purposes of the contest.

H. F. R. WATTS, M.D.,
Health Commissioner.

City Hall Annex,
Boston, Massachusetts.

REPORTS OF MEETINGS

NEW ENGLAND HEART ASSOCIATION

The regular monthly meeting of the New England Heart Association was held at the Boston City Hospital on December 13, 1937. The following program was presented:

TWO UNUSUAL CASES OF DISSECTING ANEURYSM OF THE AORTA. Soma Weiss, M.D.

Two cases of dissecting aneurysm of the aorta were presented, demonstrating (a) dissection causing compression of the coronary artery and cardiac infarction and (b)

simultaneous presence of syphilis and dissecting aneurysm. Both are reported in detail in this issue of the *Journal*.

THE CARDIOVASCULAR EFFECTS OF INTRAVENOUS INJECTIONS OF FIFTY PER CENT DEXTROSE AND SUCROSE IN NORMAL PERSONS AND IN PATIENTS WITH HEART FAILURE. Laurence B. Ellis, M.D.

An investigation was made of the effect on the circulation of the intravenous injection of 100 cc. of 50 per cent glucose or sucrose solutions. Studies were made on 27 subjects. These fall into three general groups. The first comprises 6 subjects with normal cardiovascular systems. The second consists of 10 cardiac patients without edema, including 2 who had recently had severe coronary occlusions, 2 who had never experienced heart failure, 3 who had recently recovered from congestive failure and 3 who were in definite failure without peripheral edema. The third group of 11 cardiac patients all had severe congestive failure with edema which varied in degree from moderate to massive. The cardiovascular effects of the intravenous injection of dextrose or sucrose solutions are similar. There was no significant change in the arterial blood pressure or in the heart rate. The venous pressure tended to rise during the course of the injection, and this increase was as much as 7 cm. of water. In most instances it fell progressively after the injection had stopped. The plasma volume was increased at the end of a half hour on an average of 9 to 12 per cent, or about 300 cc., and in some instances by as much as 20 per cent, or 600 cc. This increase in plasma volume is due to the drawing of fluid from the tissue spaces to the blood stream by the hypertonic action of the sugar introduced. The dilution of the plasma was temporary and had usually disappeared at the end of one hour. No significant differences in the response of the circulation could be detected which depended on the degrees of heart failure.

FRIEDLANDER'S BACILLUS PERICARDITIS. James M. Faulkner, M.D.

A man of forty-nine, who was a heroin addict and an alcoholic, entered the hospital with a history characteristic of the onset of pneumonia three days before. On admission, he presented signs of consolidation at the base of the right lung, fever, prostration and leukocytosis. The sputum contained many large, gram-negative rods, and on culture Friedländer's bacilli were the predominant organisms. The same bacterium was recovered from the blood culture on the day of admission, and subsequently from pleural exudate on both sides. For four weeks there was gradual clinical improvement with subsidence of fever and leukocytosis. The pulse rate remained elevated, however, and the electrocardiogram showed pronounced changes in the T wave. Orthopnea, increased venous pressure, enlargement of the liver, and general anasarca developed. Finally, rales appeared in the lungs and he died suddenly sixty days after admission.

Postmortem examination revealed, in addition to areas of bronchopneumonia with marked fibroblastic proliferation in the lung and pleura, a very much thickened and adherent pericardium, which cut with difficulty. There was 300 cc. of purulent exudate in the pericardial cavity. Microscopically, the pericardium consisted of fibroblasts diffusely infiltrated with lymphocytes and macrophages. The histologic appearance of the pericardium was consistent with a lesion of less than nine weeks' duration.

The case illustrates an unusual form of acute pericarditis which went on to the obstructive form of adherent pericardium in a relatively short period of time.

THE MYOCARDIUM IN FATAL CASES OF HEMOLYTIC STREPTOCOCCUS INFECTIONS. G. Kenneth Mallory, M.D., and Chester S. Keefer, M.D.

The sections of myocardium from cases dying from scarlet fever, erysipelas, streptococcus sore throat and surgical *Streptococcus hemolyticus* sepsis were studied, and the changes found were illustrated by lantern slides. These changes consisted of focal accumulations of lymphocytes, plasma cells and histiocytes beneath the endocardium, in the perivascular areas and between the muscle fibers. In several more acute cases, organisms (cocci) without reaction or organisms with an acute reaction of polymorphonuclear leukocytes were found. These lesions had the same distribution as those already described. Similar reactions, both acute and chronic, were found in other organs, particularly the kidney, liver, pancreas and adrenal.

These changes were found in 61 per cent of the hearts examined. The lesions were similar and equally common in all age groups. They were commonest and most marked in patients dying from six to ten days after the onset of the infection, but were found as late as the thirtieth day. The majority of the cases had a positive blood culture for *Streptococcus hemolyticus* at the time of autopsy.

In conclusion, it was stated that the lesions described may be infectious in origin and the result of the reaction of the tissues to the presence of invading organisms and not, as other workers have suggested, a reaction to a circulating bacterial toxin. It was felt, however, that the degree of this reaction may be somewhat enhanced as a result of antigen-antibody response.

INFARCTION OF THE HEART: A MORPHOLOGICAL AND CLINICAL APPRAISAL OF 300 CASES. William B. Bean, M.D. (presented by Paul Kunkel, M.D.).

A detailed study of 300 autopsied cases of cardiac infarction at the Boston City Hospital was made. The material was discussed under three titles: (1) predisposing and precipitating conditions; (2) clinical and morphological observations; (3) clinical course and morphological findings.

All possible correlations of the assembled data on these cases were made. These included distribution by decades, which showed that initial infarction in both men and women was highest in the seventh decade. Initial infarction in hypertensives was higher in the sixth and seventh decades, as compared with the whole group, as was also the case in those with family history of vascular disease. There was a low incidence of initial attacks and deaths during the summer months. A study of the occurrence of various types of arteriosclerosis showed that the overwhelming majority of cases presented coronary artery disease, and that 20 per cent of the infarcts followed arterial narrowing without thrombosis. The importance of surgical and medical shock was stressed as an occasional precipitating factor. A third of all cases presented pre-existing cardiac failure, and in this series dyspnea and edema did not protect from anginal pain. Alcohol and tobacco seemed to play an unimportant role, excepting perhaps alcoholic coma. Other correlations included coexisting diseased states, of which diabetes mellitus and gall-bladder disease were conspicuous. An analysis of circumstances at onset of infarction indicated that time of day, occupation and activity were unimportant factors. The majority of patients died of congestive failure.

THE EFFECT OF EPINEPHRIN AND PITRESSIN IN SODIUM-NITRITE COLLAPSE. Eugene A. Stead, Jr., M.D., and Paul Kunkel, M.D.

Epinephrin and Pitressin are drugs which are frequently used in the treatment of collapse and shock. Since controlled observations are difficult to make in patients who are critically ill, it was necessary to find a type of collapse which would reproduce the circulatory changes observed in clinical shock and which could be produced at will. Sodium nitrite in the upright position produces the manifestations of collapse ending in syncope by increasing the venous distensibility with resulting pooling of the blood in the lower part of the body. The arterioles are constricted but tissue anoxia results as the venous return to the heart decreases. (See Wilkins, R. W.; Weiss, S., and Haynes, F. W.: *J. Clin. Investigation 17,* 41-51, 1938.)

Epinephrin and Pitressin are not effective in preventing sodium-nitrite collapse. In fact, they tend to precipitate it. They do not cause enough constriction of the venules to overcome the pooling of blood in the dependent portions of the body, but do produce marked arteriolar constriction and a decrease in blood flow as measured in the hands. This increases tissue anoxia and heightens the collapse. The fact that with epinephrin and nitrite the symptoms of collapse often occur with the blood pressure at higher levels than with nitrite alone indicates that the level of arterial pressure is not a sure guide to the condition of the patient.

REPAIR IN CORONARY SCLEROSIS. Timothy Leary, M.D.

From a study of 200 advanced lesions in 120 cases of coronary disease it became evident that every advanced atherosclerotic lesion is vascularized. On the contrary, the early lesions are not vascularized. Nutrition of the normal intima is by diffusion of material from the blood in the lumen. This diffusion is adequate to care for the nutrition of early atherosclerotic lesions as well. When a lesion enlarges to the point at which diffusion nutrition ceases to be adequate, necroses occur. If the lesion is to enlarge beyond this point, a new source of nutrition, that is, by vascularization, is necessary. Vascularization in young individuals frequently arises directly from the lumen, in the form of a capillary circulation which does not tend to differentiate further. The persistence of this central, capillary circulation well into the middle period of life in many cases suggests that it may lengthen life, perhaps by ensuring nutrition to the portion of the lesion most exposed to injury that may result in thrombosis. In older persons vascularization arises from the vasa vasorum, and differentiation into arteries and veins usually occurs as the lesions age. Hemorrhage in coronary lesions originates from these new vessels, and is usually terminal. Since it arises from vessels which are produced in the repair of well-established and enlarging, atherosclerotic lesions, hemorrhage cannot be the source or cause of atherosclerosis. Repair of thrombosed vessels by canalization may in rare cases re-establish in considerable degree the crippled, local circulation.

THE CONGRESS ON MEDICAL EDUCATION

The Thirty-Fourth Annual Congress on Medical Education and Licensure was held in Chicago on February 14 and 15 of this year and while little new was presented, there was renewed emphasis on one of the principles of medicine which was dwelt on last year: namely, that the quality of the person who renders medical service is of prime importance. From time to time the emphasis has shifted: premedical education, the medical curriculum, the faculty, the mechanics of education as it concerns plant and equipment, whether in the school itself or in the hospital, and finally, the person to be educated.

The opening address was by the chairman of the Council on Medical Education and Hospitals, Dr. Ray L. Wilbur, of Stanford University, who began with a reference to the recently completed study of medical schools in the United States, the results of which have not yet been made public. Many deficiencies have been found, but it has been thought wise to refrain from giving publicity to the parts of the report showing such deficiencies before the schools themselves have been given opportunity to make good. In general the schools have shown great willingness to follow the recommendations of the Council. Uniformity in method or procedure or curriculum has not been sought, but an effort has been made to set forth a reasonable minimum for each school, taking into consideration all the resources of the school, and most important of all, what may be expected of every physician who holds himself out as qualified to treat the sick: both tangibles and intangibles must be considered. It is elementary that perhaps the most important fact in determining what comes out of a medical school is what goes in. If only poor material goes in, the school is doomed to failure.

The Council has made certain recommendations. The first is that the minimum requirement of two years of college work be raised to three. The percentage of graduates of medical schools who have actually had three years of premedical work has been steadily rising in recent years and is now over 90.

The reasons given for this recommendation are several. In the first place, although the mere length of time spent in college is not a good test of fitness, the additional time may be used to give a more nearly adequate testing of the material. We are too often deceived, or deceive ourselves, by formal standards. There is the oft-repeated statement that each year about 12,000 candidates try to squeeze themselves into 7000 places in the entering classes in medical schools, and that of the rejected 5000 many would be accepted if the schools were larger. But a more intensive study of the real qualifications of those accepted suggests that perhaps not more than 4500 are really well qualified to undertake the study of medicine.

Modern scientific medicine requires for its understanding more knowledge of the fundamental sciences on which it is built, and more of the sciences allied to the basis of professional activities. Employing two words in a narrow and popular and therefore inaccurate and perhaps misleading sense, the physician needs science and culture in his education. Science of course may be cultural, but what the physician needs is an understanding of the human body as a very complex machine and an understanding of the human being as an infinitely complex personality. Two years in a special premedical course, whether in junior college or in some other type of institution, do not ordinarily give a sufficiently wide and deep foundation for the heavy superstructure of purely professional education. There are those who think that four years in college are not too much, but the wisdom of adopting this as a minimum requirement for all is questioned.

As something over 95 per cent of all graduates of medical schools now take an internship before entering practice there has been a tendency to make such apprenticeship a formal requirement. One finds confusing tendencies, as the payment in some institutions of substantial salaries to interns. One should keep in mind the various purposes of the internship and should emphasize that which in the

long run will give the best result. The ideal is the education of the intern. That the ideal cannot be pursued uncompromisingly is evident at once, because every hospital of 100 beds certainly needs the services of the intern, but a hospital is not primarily an educational institution for any group. Such education, whether of medical student, intern, nurse, teacher or administrator, is a secondary function which many hospitals may never be able to perform in a satisfactory manner. It is, however, well established that patients in a hospital will receive better care, if, other things being equal, the hospital participates in some form of education. If interns are paid a substantial salary, the hospital is likely to think that its obligation closes with the sending of the pay check, and deterioration of the medical education of the intern is sure to follow.

One of the crying needs is an authoritative determination of when a "specialist" is not a specialist. "Self-anointed" specialists are all too common. It may be that governmental regulation will be the best method of control, but the voluntary specialist examining boards, of which there are now twelve, have begun a noteworthy and valuable service. Already their influence has been important in clarifying some of the issues involved in graduate medical education but their work lies chiefly ahead of them. They are confronted by at least one danger, that of regarding themselves, as did the medical guilds, as formed for the purpose of protecting themselves.

If one surveys the whole field of the healing art, the widespread interest in it on the part of the public, and the vast complexity of its problems as an integral part of the life of society, one comes to the very simple conclusion that what medicine needs most, in order that the profession may meet its responsibilities, is character and brains and leadership. It is the part of medical education to discover, select and train, in such ways as may be possible, physicians who not only minister to the needs of individuals but also are able to take their proper place as advisers and participators in shaping the policies of the communities, whether small or large, of which they are a part.

It is not likely that the problems of professional licensure will be easily solved in the best way by the efforts of one profession alone, and the general problems of this nature were discussed by Mr. John K. Clark, of the New York Board of Law Examiners. In spite of the many differences of background of lawyer and physician, one of which is that the lawyer practices as an officer of the court and therefore under the judiciary while the physician is licensed under legislative authority, certain common principles of qualification exist, such as knowledge of the principles of the subject, ability to analyze a complicated state of affairs and to select the principles which apply to the specific problems involved, skill in the application of these principles, and ability to make a clear statement of the application. But the determination of fitness, the prime function of a licensing board, has its chief difficulty not in the field of acquisition of knowledge by the candidate but in the field of character. Here the opportunities for insight in medicine are much greater than in law, because of closer contact of student and teacher in laboratory and clinic and especially in hospital. In the law school much of the instruction is didactic. In law as in medicine the character of the candidate is of crucial importance, and in New York co-operation between school and licensing authority in an effort to determine the character of the applicant has been helpful. In some law schools, however, and especially in the part-time schools, the teachers know practically nothing about the students in this very important respect. One serious difficulty in determining what kind of lawyer, for example, the candidate will prove to be, is that character development is not complete at the age of twenty-one or twenty-two. Better insight is needed, based on better acquaintance, and the procedure in Pennsylvania will perhaps be helpful. There, each candidate for a law degree is assigned to a practicing lawyer whose duty it is to make a personality study. He may be in a position to do some teaching, especially in giving the right point of view in approaching the practice of law, some evaluating, and some advice and direction. It has been found that a substantial percentage of the candidates are advised not to go on in the course.

A strong plea was made by Father Alphonse M. Schwitalla, of St. Louis, for closer incorporation of the medical school in the university, for both can profit greatly by close association. It is not clear which would profit more, probably varying with conditions, but each has a significant contribution to make to the solution of their common problems. In the association are two dangers: too much federalization and too much individualization. Perhaps the most important field in which the university can be of help is to make clear the social implications and obligations of medicine.

In recent years the problem of specialism in medicine has received considerable attention. It is not new, however, and Dr. Willard C. Rappleye, of New York, noting the proposed requirement of three years of collegiate work before entrance to the medical school, reminded the Congress that if this becomes effective in 1940 it will be on the 800th anniversary of the requirement by Roger, of Sicily, that three years of college work should precede the beginning of the study of medicine in the university of his day. It is interesting to note how thought in one field may fertilize another related field. Study of the needs of the specialist examining boards helps to make clear the needs of graduate education and the need in the specialties for persons with better training in the fundamentals of the undergraduate medical course and in the premedical fields. From this study came Dr. Rappleye's suggestion that for better co-ordination and co-operation of all medical interests there should be formed a national medical council — non-governmental in nature, advisory in function — to make a further study of the preparation of the physician for his work. The suggestion is worthy of careful consideration by the whole medical profession and by all persons interested in the future health program of the entire country.

The proposal to limit student enrollment in medical schools always stimulates controversy so that it is difficult to get a consideration of the subject on its merits. Dr. Walter M. Kotschnig, of Smith College, presented an excellent exposition, perhaps because he was not handicapped by being a physician. He pointed out what has been noted before, especially by non-medical students of the subject, that while the limitation in a given school may be reasonable if it is based on the real capacity of the school, a general limitation because someone thinks that there are too many doctors has nothing actual to support it, because an accurate determination of how many physicians are needed has never been made. There should be a scientific definition of the demand and some sort of calculation of future demands, which can be at best only an approximation. It may be that some restraint should be exercised as a result of previously made scientific determinations, but such restraint should be characterized by lack of constraint and should be based on comprehension of all available information. The studies should be made not by but with persons of the professional group, for on ac-

count of possible results, the profession might be regarded as prejudiced in favor of restriction. After all, the greater need is for improvement of the physicians rather than for increase or decrease in their number.

Various limited aspects of the undergraduate teaching of medicine were discussed: clinical medicine by Dr. Burrell O. Raulston, California; preventive medicine by Dr. J. G. FitzGerald, Toronto; obstetrics by Dr. James R. McCord, Georgia; and nutrition by Dr. Salvatore P. Lucia, California.

One morning was devoted to a symposium on graduate medical education, a subject to which more attention has been directed each year recently. If one notes what is done now, compared with fifteen years ago, astonishing progress has been made. But if one considers what the specialist examining boards think advisable in the preparation of their diplomates, one sees that only a beginning has been made. In these discussions the needs of the general practitioner for continued preparation received constant attention.

Two sessions were devoted to problems which especially concern state boards of licensure. Since internships are now taken by over 95 per cent of the graduates of medical schools each year and since there are many more internships available than there are candidates to fill them, it has been suggested that one year of internship be required by law before admission to examination for registration. Twenty states either have already made or will soon make this requirement. At first sight the proposal seems reasonable, but closer study makes it evident that the matter is not so simple as it appears. How much is the internship worth? What kinds of internship are available? What kind of internship is desirable? Two ideas dominate the situation, and they are not immediately compatible without qualification: the internship is for the further education of the physician — the internship is for the purpose of getting some necessary hospital work done.

It is well known that there is exploitation of interns; this follows from the fact that the hospital takes no responsibility for seeing that the intern is given the opportunity to make the most of his experience. In some of the so-called teaching hospitals, that is, those which are identified with medical schools and in which teaching of undergraduate medical students is constantly carried on, carefully planned courses for the training of interns are provided. But such hospitals are relatively few, and if it is difficult to find enough teachers of medicine to man the teaching hospitals. What hope is there that hospitals remote from medical schools will have adequate teachers for interns?

A question on which there is vigorous controversy is the requirement by some boards of registration that the year of internship be on a rotating service. The result is that some states will not accept the one-year straight internship, which is the kind of experience received in the teaching hospitals by the best of the recent graduates. To what extent this is militating against the admission to practice in these states of the better grade of physician is not clear, but if the regulation is rigorously enforced, it will undoubtedly have a deleterious effect. In this controversy what is usually forgotten is that the mechanics of education is of less importance than the personal quality of the teacher. The hospitals remote from the medical schools do not as a rule have on their staffs physicians who are interested in teaching. Until hospitals more generally recognize and accept a responsibility for educating the interns, it is generally agreed that it is unwise to require the internship before admission to examination.

The problems presented to state boards of registration by candidates who have received their medical education abroad and who seek admission to practice in the United States are numerous and vexatious. It is not so much that the standards for admission to practice in foreign countries have been appreciably lowered, but that often the persons who make application for registration in the United States have not been permitted to fulfill all the requirements for entering practice in the country in which the school is situated. Sometimes they have been allowed to take all the courses and examinations but for racial reasons have been refused degrees, or have been refused licensure in the country in which they studied. Often clinical opportunities have been restricted to certain groups, or the course given to foreigners has been different and less rigid than that given to nationals. There is urgent need for some uniformity of procedure in evaluating the credentials from foreign medical schools.

One example of what can be done in a limited field was given by Dr. William C. MacTavish, of New York, who in co-operation with a small group of interested persons has been securing information about American students in Italian medical schools. When in 1933 there were published the rulings of the American Medical Association and of the Federation of State Medical Boards with reference to accepting Americans who had studied in foreign medical schools, there was expressed resentment on the part of a considerable element in the Italian-born American population at the alleged reflection on Italian medical schools. It required long-continued, patient and tactful negotiations, in which the official Italian representatives were most co-operative and fair-minded, to reach the present satisfactory arrangement. American students who wish to study medicine in Italian schools are required to file their credentials with the nearest Italian consul. The papers are forwarded to the Italian Consul-General in New York and are evaluated by Dr. MacTavish as they would be for an approved medical school in the United States, except that the candidate must show sufficient knowledge of Italian to be able to profit by his study abroad. By this procedure many persons who are unsuited are prevented from going. For the benefit of those who are accepted, sixty-five internships in Italian hospitals are reserved. The Italian authorities have expressed themselves as much gratified with the distinct improvement in the candidates from the United States admitted under the present procedure, as contrasted with those under the previous unsupervised method. It is an example of what can be accomplished by intelligent effort.

There was a symposium on the promulgation of regulations authorized by law, and a résumé of the effects of the basic science law in Minnesota, which include a considerable reduction in the number of new registrants in osteopathy and chiropractic. There is no general agreement that this procedure is the best way of dealing with the problem presented by the cults.

NOTICES

AMERICAN ASSOCIATION FOR THE STUDY OF GOITER

The American Association for the Study of Goiter, pursuant to its accepted invitation and to correspondence with the honorary presidents and attending members of the First and Second International Goiter Conferences, announces that the Third International Goiter Conference is to convene in Washington, District of Columbia, September 12 to 14.

The subjects proposed for discussion are as indicated in the outlined tentative program given below.

Physicians and others in the United States and in other countries desirous of participating in the program are requested to submit titles at their earliest convenience. Since the time which it is possible to allocate on the program is obviously limited, it will be necessary for the Program Committee to exercise its best judgment in the selection of speakers and to insist without exception that the speakers conform to the time allocated.

Manuscripts of addresses, papers and discussions delivered or read at the meetings are to be published in extenso in the form of transactions.

The official language of the conference will be English. Interpreters will be furnished for papers read in other languages.

For further information concerning the conference, communicate with the chairman of the Program Committee (Allen Graham, M.D., 2020 East 93 Street, Cleveland, Ohio).

* * *

OUTLINE OF TENTATIVE PROGRAM

First Day. Subjects: Endemic Goiter, Cretinism and Myxedema.

Etiology	Iodine
Pathology	Prophylaxis
Types	Thyroiditis
Geographic distribution	Malignant goiter

Second Day. Subjects: The Thyroid in Relation to Metabolism, Nutrition and Endocrine Glands: Physiological and pathological interrelation and clinical application.

Oxidation	Parathyroid
Sugar metabolism	Pituitary
Water balance	Adrenals

Third Day. Subject: Hyperthyroidism.

Basal metabolism	Types:	Diffuse toxic goiter
Iodine		Nodular toxic goiter
Complications		
Recurrences	Treatment:	Nonsurgical
Goiter heart		Surgical

The subdivisions under the subjects above are for illustrative purposes only and are not to be considered as all-inclusive or exclusive.

CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Orthopedic Consultant
Lowell	April 1	Albert H. Brewster
Salem	April 4	Harold C. Bean
Haverhill	April 6	Arthur T. Legg
Gardner	April 12	Mark H. Rogers
Brockton	April 14	George W. Van Gorder
Worcester	April 15	John W. O'Meara
Pittsfield	April 18	Francis A. Slowick
Springfield	April 20	Garry deN. Hough, Jr.
Fall River	April 25	Eugene A. McCarthy
Hyannis	April 26	Paul L. Norton

NEW BEDFORD CANCER CLINIC

The New Bedford Cancer Clinic in conjunction with the State Cancer Commission will hold a public demonstration clinic of cured cases of cancer at the Outpatient Department of St. Luke's Hospital, New Bedford, on Wednesday, April 13, at 4:00 p. m.

All physicians in this district are invited to attend the clinic.

Curtis Tripp, M.D., *Secretary.*

TUFTS MEDICAL ALUMNI DINNER

The annual dinner of the Alumni Association of Tufts College Medical School will be held Wednesday, March 30, at 7:00 p. m. at the Copley-Plaza Hotel, Boston.

For reservations call Hub. 9670.

Robert T. Phillips, M.D., *Secretary.*

MASSACHUSETTS MEMORIAL HOSPITALS

The annual reunion of the House Officers' Alumni Association of the Massachusetts Memorial Hospitals will be held on Saturday, April 23, at 10:00 a. m. in the Collamore Memorial Building.

Welman B. Christie, M.D., *Secretary-Treasurer.*

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Beth Israel Hospital, on Monday, March 28, at 8:15 p. m.

PROGRAM

The Incidence of the Criteria of Allergy in Cases of Cardiac Asthma. Dr. Hyman Morrison.

The Significance of Electrocardiographic Changes During Attacks of Angina Pectoris. Dr. Joseph E. F. Riseman.

The Relation of Blood Pigment Metabolism to the Changes in Blood Volume in Congestive Heart Failure. Dr. John Waller.

The Effect of Digitalis in Partial Heart Block. Dr. Mark D. Altschule.

The Clinical and Pathological Manifestations of Coronary Arterial Disease as Disclosed by Injection Plus Dissection Studies. Dr. David Davis.

The Breath-Holding Test: A simple standard stimulus for blood pressure. Dr. David Ayman.

Cardiac Cirrhosis. Dr. Herrman L. Blumgart.

Interested physicians and medical students are invited to attend.

James M. Faulkner, M.D., *Secretary.*

HAMPSHIRE DISTRICT MEDICAL SOCIETY

The annual meeting of the Hampshire District Medical Society will be held at the Dickinson Hospital, Northampton, on Wednesday, May 11, at 11:30 a. m.

Joseph D. Collins, M.D., *Secretary.*

BOSTON SOCIETY FOR THE ADVANCEMENT OF GASTROENTEROLOGY

The next meeting of the Boston Society for the Advancement of Gastroenterology will be held at the Carney Hospital, on Wednesday, March 30, at 12 o'clock noon.

Case demonstrations will be given by Drs. Louis F. Curran, A. McKay Fraser, William E. Browne, Edward Leonard and Norman A. Welch, of the medical and surgical staffs.

Physicians, medical students and nurses are cordially invited to attend.

Charles W. McClure, M.D., *Secretary.*

THE JOHN T. BOTTOMLEY SOCIETY

The John T. Bottomley Society of the Carney Hospital Outpatient Department will hold its regular monthly meeting on Tuesday, April 5, at 11:30 a. m.

Dr. Laurence McGrath will speak on "Allergy."

William J. Macdonald, M.D., *Secretary.*

TUMOR CLINIC, BOSTON DISPENSARY

Each Tuesday and Friday morning from ten to twelve-thirty there is a meeting of the Tumor Clinic of the Boston Dispensary, a unit of the New England Medical Center. All kinds of tumors are seen, discussed, and when indicated, treated with radium and high-voltage x-ray.

Physicians are welcome to visit this clinic and bring a patient to the clinic for diagnosis.

RADIO BROADCASTS

The seventh group of weekly broadcasts sponsored by the American Medical Association and the National Broadcasting Company concern health education. These dramatized health messages are intended to furnish supplementary material for health teaching in junior and senior high schools and are broadcast every Wednesday from 2:00 to 2:30 p. m. over the Red Network. The dates and subjects are as follows:

March 30 — A Fool for a Day. Fallacies and popular beliefs that are not true and that influence behavior in a manner detrimental to health.

April 6 — Living with People. Elements of mental hygiene; getting along with people; adjustment to the environment.

April 13 — It May Happen to You. Accidents in the home and on the highway and ways to avoid them.

April 20 — Who Chooses Your Doctor? The characteristics of a reputable physician as distinguished from cults, quacks, fakers, faddists or exploiters.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Monday, March 28

Monday, March 28

*8:15 p. m. New England Heart Association. Beth Israel Hospital.

Tuesday, March 29

*9-10 a. m. Boston Dispensary. A Clinical Evaluation of the Blood Sedimentation Rate as a Routine Diagnostic Procedure. Dr. Elbert B. Agnor.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

Wednesday, March 30

*9-10 a. m. Boston Dispensary. Hospital case presentation. Dr. S. J. Thannhauser.

*12 m. Clinicopathological conference. Children's Hospital amphitheater.

*12 m. Boston Society for the Advancement of Gastroenterology. Carney Hospital.

7 p. m. Tufts Medical Alumni Dinner, Copley-Plaza Hotel, Boston.

Thursday, March 31

8:30-9:30 a. m. Exchange visit, surgical and orthopedic staffs of the Peter Bent Brigham and Children's hospitals, held this week at the Children's Hospital.

*9-10 a. m. Boston Dispensary. Interesting Clinical Problems from the District Service. Dr. Isadore Olef.

Friday, April 1

*9-10 a. m. Boston Dispensary. Specific Therapy for Certain Anemias of Childhood. Dr. Louis K. Diamond.

*10 a. m. - 12:30 p. m. Tumor clinic. Boston Dispensary.

12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital, Ether Dome.

Saturday, April 2

*9-10 a. m. Boston Dispensary. Pneumonia. Dr. Joseph H. Pratt.

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Henry A. Christian.

Sunday, April 3

4 p. m. Illustrated, public, health lecture, Faulkner Hospital auditorium. "Nerves" and Their Relation to Insanity. Dr. Merrill Moore.

*Open to the medical profession.

March 25 — Staff meeting of the Massachusetts Memorial Hospitals, 8:15 p. m.

March 28 — New England Heart Association. Page 546.

March 28 - April 1 — Postgraduate Institute of the Philadelphia County Medical Society. Page 282, issue of February 10.

March 30 — Tufts Medical Alumni Dinner. Page 546.

March 30 — Poston Society for the Advancement of Gastroenterology. Page 546.

April 1-8 — Springfield District Teaching Clinics. Page 499, issue of March 17.

April 4-8 — The American College of Physicians. Page 41, issue of July 1.

April 5 — Greater Boston Medical Society. 8:30 p. m., auditorium of Beth Israel Hospital, Boston.

April 5 — John T. Bottomley Society. Page 546.

April 13 — New Bedford Cancer Clinic. Page 546.

April 13 — Eastern Hampden Medical Association. Page 499, issue of March 17.

April 14 — Pentucket Association of Physicians. Hotel Bartlett, 95 Main Street, Haverhill, 8:30 p. m.

April 18 — Boston Medical History Club. Boston Medical Library, 8 Fenway, Boston.

April 18, 19 and 20 — Thomas William Salmon Memorial Lectures. Page 450, issue of March 10.

April 23 — Massachusetts Memorial Hospitals, annual reunion of house officers' alumni association. Page 546.

April 26 — New England Society of Psychiatry. Page 322, issue of February 17.

May 31, June 1 and 2 — Annual meeting of the Massachusetts Medical Society. Hotel Bradford, Boston.

June 6, 7, 8, and 9 — American Association of Industrial Physicians. Page 499, issue of March 17.

June 13-17 — American Medical Association. San Francisco.

June 13, October 8 and November 15 — American Board of Ophthalmology. Page 282, issue of February 10.

September 12-14 — American Association for the Study of Goiter. Page 545.

October 17-21 — Clinical Congress of the American College of Surgeons, New York City.

October 24-26 — Academy of Physical Medicine, Scientific Session. Washington, D. C.

District Medical Societies

BRISTOL SOUTH

May 5 — 5 p. m., New Bedford.

ESSEX SOUTH

April 6 — Gloucester Hospital, Gloucester. Clinic at 5 p. m. Dinner at 7 p. m. Speaker and subject to be announced.

May 5 — Censors meet at Salem Hospital, 3:30 p. m.

May 11 — Annual meeting, Salem Country Club, Peabody. Dinner at 7 p. m. Speaker and subject to be announced.

FRANKLIN

Meeting will be held at the Franklin County Hospital, Greenfield, at 11 a. m. the second Tuesday of May.

HAMPDEN

Meetings will be held on the fourth Tuesday in April and July.

HAMPSHIRE

May 11 — Page 546.

MIDDLESEX EAST

Meeting will be held at the Bear Hill Golf Club, Stoneham, at 12:15 p. m. on May 11.

MIDDLESEX NORTH

Meeting will be held at the Vesper Country Club, Lowell, on April 27.

NORFOLK DISTRICT

March 29 — Page 500, issue of March 17.

May — Annual meeting.

The censors meet on the first Thursdays of May and November in each year.

NORFOLK SOUTH

Meetings held at 12 noon.

April 7 — At the Quincy City Hospital.

May 5 — Annual meeting.

PLYMOUTH

Meetings will be held at 11 a. m. on April 21, May 19 and July 21.

WORCESTER

April 13 — Hahnemann Hospital, Worcester. Dinner will be at 6:15, to be followed by business session and scientific program.

May 11 — Afternoon and evening, annual meeting. Place and schedule of program to be announced.

BOOK REVIEWS

Diathermy: Including diathermotherapy and other forms of medical and surgical electrothermic treatment. Elkin P. Cumberbatch. Third edition. 576 pp. Baltimore: William Wood & Company, 1937. $6.00.

The author of this book, an Englishman, is one of the few living men who have worked with electrotherapy from its beginning. He is thoroughly conversant with diathermy of the "long-wave" (300 meter wavelength) type, which uses metal electrodes in contact with the body. A large portion of the book is devoted to that type of current. Unfortunately, this procedure is being used less and less, and manufacturers in this country have practically stopped making such machines.

The book is divided into three parts: (1) "Physical and Electrotechnical Principles," (2) "Medical Electrothermic Methods and Their Uses," (3) "Surgical Electrothermic Methods and Their Uses." The chapters dealing with the physics of the high-frequency currents, largely written by Dr. H. J. Taylor, physicist to the Institute of Physical Medicine, are excellent for those desirous of knowing how high-frequency apparatus is made and what may be expected by its use. Unreasonable space has been allotted to subjects which would be clearer and more readable if fewer pages had been written. For instance, a chapter of forty pages is devoted to a discussion of recorded body temperatures following the long-wave type of diathermy. Three hundred and ten of the five hundred and fifty pages are devoted to long-wave diathermy and its relation to medical procedures. The balance deals with surgical procedures, largely by the older method. Only fifty pages are given to theory and an inadequate allusion to the short-wave diathermy.

There is much repetition occurring throughout. Far too much space has been allotted to the elementary details, while frequently not enough definite scientific information has been given to more important aspects. It is thoroughly unsatisfactory as a textbook on diathermy here in America where we have largely discarded long-wave diathermy and are bending our energies toward proving what seems to be advantageous in the short-wave field.

The real usefulness of this book lies in the help it offers teachers in obtaining details of the history of high-frequency currents, some of their applications, and — perhaps most important of all — their physics.

Alcohol: One man's meat. Edward A. Strecker and Francis T. Chambers, Jr. 230 pp. New York: The Macmillan Company, 1938. $2.50.

This is a volume written by Dr. Strecker with the assistance of a former patient. It approaches the problem from a psychological aspect, which method of attack is in accord with the best medical opinion of the day. The treatment of alcoholism is a matter for the attention of a psychiatrist preferably, yet regularly all medical men are confronted with the problem of how to handle situations in which the abuse of alcohol looms large.

Normal and abnormal drinkers are discussed and the drives motivating them are examined in terms of adjustment, not to alcohol itself but rather to the background of the drinker. The inheritance of a nervous system which is non-resistant to alcohol is not held a bar, by the authors, to a routine of activity and achievement. It is their contention that there are no half-measures possible for the alcoholic. He must avoid even a single drink since his resistance, but not necessarily his physiological tolerance, is so much below the average man's threshold.

Approximately one half the book is devoted to a discussion of the treatment of alcoholism. Acknowledgment is made to the late Richard Peabody, of Boston, and the lines laid out for a therapeutic rationale closely approach those devised by him.

Manual of Clinical and Laboratory Technic. Hiram B. Weiss and Raphael Isaacs. Fifth edition, reset. 141 pp. Philadelphia and London: W. B. Saunders Company, 1937. $1.50.

This is an unusually fine little book, remarkable for the completeness with which it covers the whole field of medical examination, and showing a mastery of medicine by the authors which has come from years of experience in the laboratory and the clinic. In its fifth edition it should continue to prove useful to student, intern and practitioner.

One of its features is that it includes the newer tests not yet available in the standard textbooks and found only in current periodical literature. Among the material added in this edition are: additional tests for Bence-Jones substance; methods of counting cellular elements and of measuring the amount of vitamin C in the urine; a graph for the conversion of percentage of hemoglobin to grams; methods of calculation of various blood indices; new methods for determining the clotting and retraction times of the blood; a listing of the characteristics of the blood in pyogenic infection; methods of measuring the diameter and volume of the red-blood cells, and of oxidase staining; the technic of the sheep-cell agglutination test in infectious mononucleosis, of hydrogen-ion-concentration determinations of gastric juice and of the Neufeld reaction for pneumococcus types; methods of counting the cells of the saliva and of the bone marrow; descriptions of the Nonne-Apelt reaction, liver-function tests, the Takata-Ara reaction; the technic for determining the albumin-globulin ratio in blood serum, and for making the Congo red test for amyloidosis and diagnostic tests for undulant fever. The normal standards for each test are given, and certain details in the interpretation of tests and their clinical application are discussed. A comprehensive table of nutritive values of foods and a complete index add to the value of this manual.

A Practical Treatise on Diseases of the Skin: For the use of students and practitioners. Oliver S. Ormsby. Fifth edition, thoroughly revised. 1334 pp. Philadelphia: Lea & Febiger, 1937. $12.00.

All students of dermatology will be interested in this new edition of "Diseases of the Skin." Whereas the greater part of the material is essentially the same as in the previous edition, twenty new diseases have been described, and other material has been rewritten. New illustrations have been added, principally photomicrographs, which is indication of the growing interest in the pathology of dermatology.

The mycologic side is treated as fully as could be expected in a work of this scope. Sabouraud's standard classification of the tineas is given, but no reference is made to the newer attempts at classification.

This book is a vast storehouse of description of disease, etiology, differential diagnosis and treatment. Its possessor may feel himself fortunate in having so much information in one volume, which is easily available. A very complete bibliography is provided.